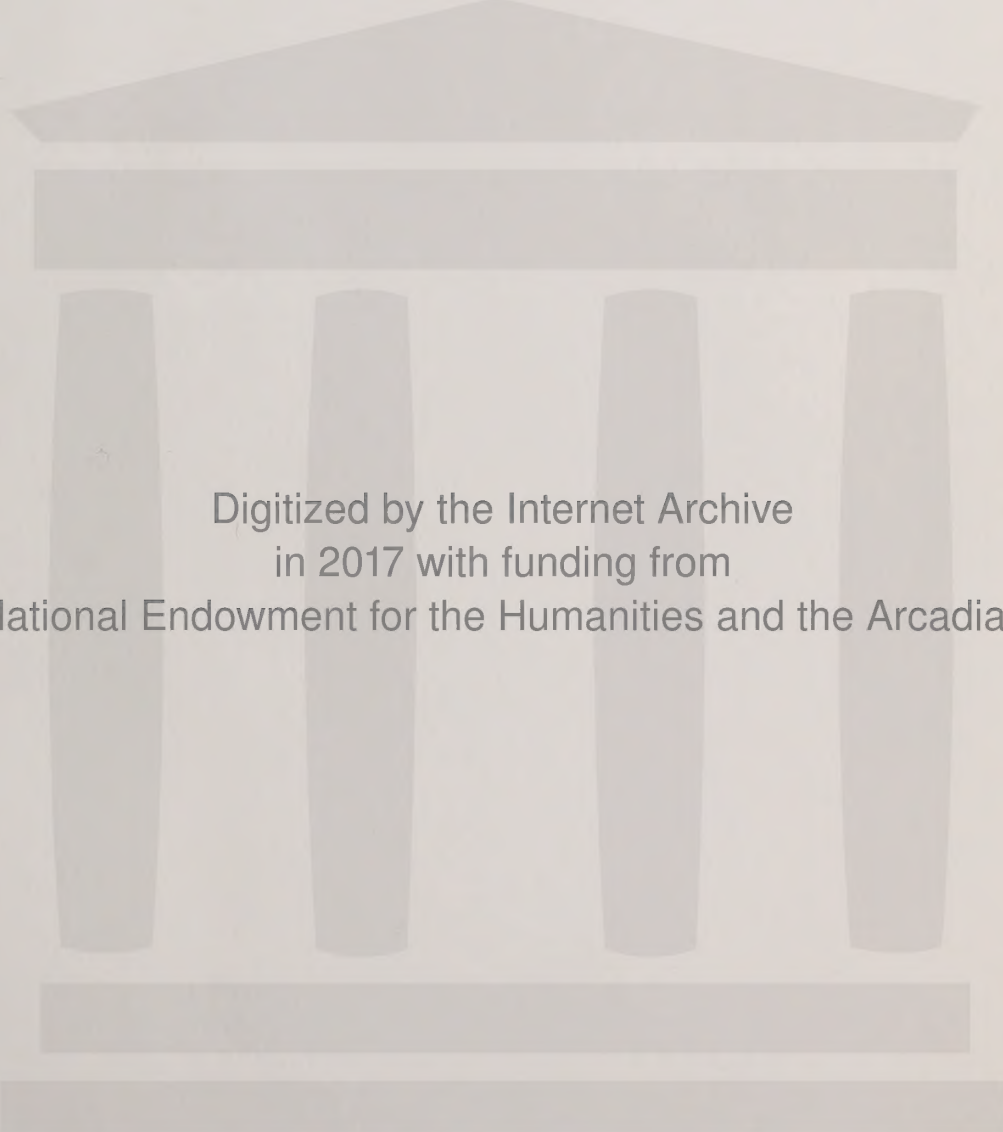


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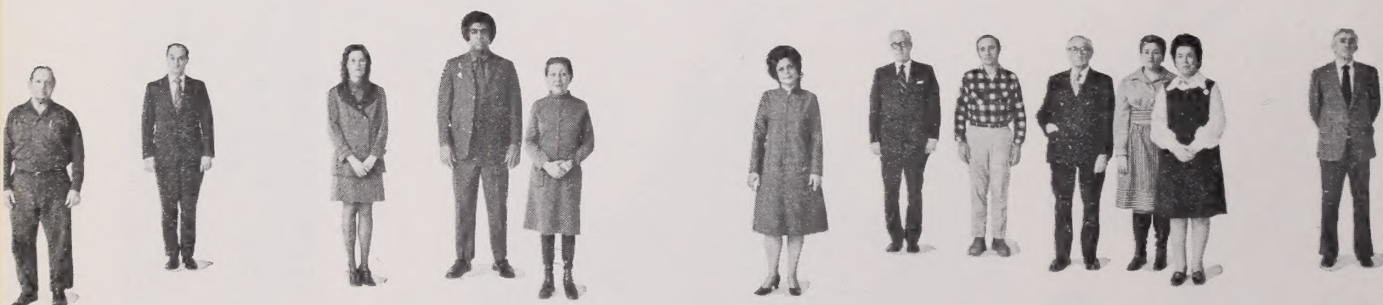
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Indications: Acute gouty arthritis, rheumatoid arthritis, rheumatoid spondylitis

Contraindications: Children 14 years or less; senile patients; history or symptoms of G.I. inflammation or ulceration including severe, recurrent or persistent dyspepsia; history or presence of drug allergy; blood dyscrasias; renal, hepatic or cardiac dysfunction; hypertension; thyroid disease; systemic edema; stomatitis and salivary gland enlargement due to the drug; polymyalgia rheumatica and temporal arteritis; patients receiving other potent chemotherapeutic agents, or long-term anticoagulant therapy

Warnings: Age, weight, dosage, duration of therapy, existence of concomitant diseases, and concurrent potent chemotherapy affect incidence of toxic reactions. Carefully instruct and observe the individual patient, especially the aging (forty years and over) who have increased susceptibility to the toxicity of the drug. Use lowest effective dosage. Weigh initially unpredictable benefits against potential risk of severe, even fatal, reactions. The disease condition itself is unaltered by the drug. Use with caution in first trimester of pregnancy and in nursing mothers. Drug may appear in cord blood and breast milk. Serious, even fatal, blood dyscrasias,

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including aplastic anemia, may occur suddenly despite regular hemograms, and may become manifest days or weeks after cessation of drug. Any significant change in total white count, relative decrease in granulocytes, appearance of immature forms, or fall in hematocrit should signal immediate cessation of therapy and complete hematologic investigation. Unexplained bleeding involving CNS, adrenals, and G.I. tract has occurred. The drug may potentiate action of insulin, sulfonylurea, and sulfonamide-type agents. Carefully observe patients taking these agents. Nontoxic and toxic goiters and myxedema have been reported (the drug reduces iodine uptake by the thyroid). Blurred vision can be a significant toxic symptom worthy of a complete ophthalmological examination. Swelling of ankles or face in patients under sixty may be prevented by reducing dosage. If edema occurs in patients over sixty, discontinue drug.

Precautions: The following should be accomplished at regular intervals: Careful detailed history for disease being treated and detection of earliest signs of adverse reactions; complete physical examination including check of patient's weight; complete weekly (especially for the aging) or an every two week blood check; pertinent laboratory studies. Caution patients about participating in activity requiring alertness and coordination, as driving a car, etc. Cases of leukemia have been reported in patients with a history of short- and long-term therapy. The majority of these patients were over forty. Remember that arthritic-type pains can be the presenting symptom of leukemia.

Adverse Reactions: This is a potent drug; its misuse can lead to serious results. Review detailed information before beginning therapy. Ulcerative esophagitis, acute and reactivated gastric and duodenal ulcer with perforation and hemorrhage, ulceration and perforation of large bowel, occult G.I. bleeding with anemia, gastritis,

epigastric pain, hematemesis, dyspepsia, nausea, vomiting and diarrhea, abdominal distention, agranulocytosis, aplastic anemia, hemolytic anemia, anemia due to blood loss including occult G.I. bleeding, thrombocytopenia, pancytopenia, leukemia, leukopenia, bone marrow depression, sodium and chloride retention, water retention and edema, plasma dilution, respiratory alkalosis, metabolic acidosis, fatal and nonfatal hepatitis (cholestasis may or may not be prominent), petechiae, purpura without thrombocytopenia, toxic pruritus, erythema nodosum, erythema multiforme, Stevens-Johnson syndrome, Lyell's syndrome (toxic necrotizing epidermolysis), exfoliative dermatitis, serum sickness, hypersensitivity angitis (polyarteritis), anaphylactic shock, urticaria, arthralgia, fever, rashes (all allergic reactions require prompt and permanent withdrawal of the drug), proteinuria, hematuria, oliguria, anuria, renal failure with azotemia, glomerulonephritis, acute tubular necrosis, nephrotic syndrome, bilateral renal cortical necrosis, renal stones, ureteral obstruction with uric acid crystals due to uricosuric action of drug, impaired renal function, cardiac decompensation, hypertension, pericarditis, diffuse interstitial myocarditis with muscle necrosis, perivascular granuloma, aggravation of temporal arteritis in patients with polymyalgia rheumatica, optic neuritis, blurred vision, retinal hemorrhage, toxic amblyopia, retinal detachment, hearing loss, hyperglycemia, thyroid hyperplasia, toxic goiter, association of hyperthyroidism and hypothyroidism (causal relationship not established), agitation, confusional states, lethargy; CNS reactions associated with overdosage, including convulsions, euphoria, psychosis, depression, headaches, hallucinations, giddiness, vertigo, coma, hyperventilation, insomnia; ulcerative stomatitis, salivary gland enlargement. (B)98-146-070-G

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VETERANS MEDICAL CARE: PAST, PRESENT AND FUTURE

John W. Walsh, MD

As a newcomer to medical care in the island of Puerto Rico, it seems important to me that I communicate to the health professions some personal ideas regarding the Veterans Administration (VA), based not only on my experience in Puerto Rico; and previous exposure in both the VA Central Office and various hospitals on the mainland; but also on my personal review and understanding of the changing medical care situation in all of the United States.

This paper will deal with the following themes as they relate to Puerto Rico and the Virgin Islands:

1. The VA has carried, and will continue to carry a greater proportion of the medical care for veterans who are considered medically indigent;
2. The VA in San Juan has a major responsibility in the education and training of health manpower;
3. The VA in all of the United States is undergoing great change.

Veterans Administration and Treatment of Medically Indigent

About 15 years ago, during the administration of President Eisenhower, there was considerable discussion of the long range goals of the Veterans Administration. Those who took a more conservative position felt that the VA should be responsible only for medical treatment for veterans who had service connected disabilities, diseases or injuries incurred in military service. Others felt that veterans with non-service connected disabilities should not be discriminated against, and that VA's future planning should take into account the hospitalization needs of all veterans. Those who favored consideration of the non-service connected veteran were conscious, of course, of the fact that there were some 15 million World War II veterans who were hardly using VA hospitals in the 1950's. They would, it was suggested, make more demands for medical care in the 1970's, when as a group they reached the age

when the incidence of cancer, diabetes, and cardiovascular - renal disease would rise very sharply.

Although this argument seems to be pure philosophy, it had important ramifications. If the policy were to provide hospital care only for service connected veterans, a comparatively small number of VA beds would be needed, perhaps 30,000. If unrestricted medical care were to be planned for all veterans, both service connected and non-service connected, the number of beds planned for construction (and this was before the Vietnam war) would have to be at least 180,000. Since it costs anywhere from \$20,000 to \$35,000 for each constructed hospital bed, it was important to decide what should be VA's long range construction goal.

As if often the case, a compromise between the two positions was taken, and President Eisenhower set 125,000 hospital beds as the long range goal. I emphasize hospital beds because future VA actions have actually diminished the importance of hospitals as the only way to provide medical care for the non-service connected veteran. Later in this article I shall have more to say on this matter.

In setting this ceiling on hospital beds constructed and operated — a position which was to be followed by Congress in its appropriation for construction — the Federal government said, "The VA has a prime responsibility to treat the service connected veteran, and an important secondary responsibility to hospitalize non-service connected veterans who cannot afford to pay for medical care outside the VA".

In recent years, the Veterans Administration has not needed 125,000 hospital beds. During the past fiscal year, its 167 hospitals in all the states except two (Alaska and Hawaii) had an average operating capacity of 96,352 beds. The daily hospital patient census was only 80,971 for the more than 28 million veterans (1).

One might ask: isn't this a very low ratio of bed utilization? With 28 million veterans and only 80,971 census, this comes to only 2.9 per 1000 population! Why, this is below the Hill-Burton construction standards of 3.5 beds per 1000 population!

From the Veterans Administration Center, San Juan, Puerto Rico.

**TABLE I: AVAILABILITY OF HOSPITAL BEDS FOR VETERANS IN
TOTAL UNITED STATES AND IN ANTILLES**

	United States as a Whole	Puerto Rico and Virgin Islands
Veteran Population (April 1972)	28,800,000	172,000
Number of hospital beds	96,350	688
— if contract beds are included	96,845	948
Hospital Beds per 1000 veteran population	3.33	4.0
— if contract beds are included	3.36	5.5

Source: *Veterans Administration*, VA Field Station Summary, June 1972, Part 3.

TABLE II: RATIO OF VETERANS TO TOTAL POPULATION IN U.S. AND ANTILLES

	United States as a Whole	Puerto Rico and Virgin Islands
Total Population	203,212,000	2,774,000
Veteran Population	28,800,000	172,000
Ratio of Veterans to Total Population	1:7	1:16

Calculated from: *U. S. Department of Commerce, Bureau of the Census*, 1970 Census of Population April 1970.

TABLE III: PER CAPITA MEDICAL CARE FOR VETERANS

	United States as a Whole	San Juan Veterans Administration
Medical Care Expenditures Fiscal Year 1972	\$2.3 billion	\$23.0 million
Total Veteran Population	28.8 million	172,000
Per Capita Expenditure Fiscal Year 1972 (Approx)	\$80	\$130

Source: *Veterans Administration*, Budget in Brief, 1972 Fiscal Year.

TABLE IV: OUTPATIENT CARE FOR VETERANS AT SAN JUAN
VETERANS ADMINISTRATION AND OTHER VA CLINICS – FISCAL YEAR 1972

	San Juan VA Outpatient Service	All VA Outpatient Clinics
Veteran Population Served	172,000	28,800,000
Number of Visits FY 1972 to VA Clinics and fee basis Physicians	153,400	8,869,000
Number of Visits per 1000 Population	888	308

Source: *Veterans Administration*, VA Field Station Summary June 1972, Part 3.

The bed ratio of beds for the veteran population is low. The need for hospital care has not been clearly demonstrated in all of the United States. Inpatient hospital care is required, of course, for the service connected veteran. In the entire country there are 2.1 million veterans who are service connected, of whom 19,000 are in Puerto Rico and the Virgin Islands (2). They form a smaller part of the total patient load. The preponderance of admissions are for non-service connected veterans who have a demonstrated need for medical care, and are unable to pay for it. Many of the admissions come from the group of veterans who, having already had economic and medical problems, receive non-service connected pensions as provided by law. Nationwide there were 1.3 million pensioners at the end of fiscal year 1972; there were 9,400 who lived in the Antilles.

The facts are that the VA provides care mainly for the medically indigent veteran. As a group, most veterans are wage earners and, as subscribers to prepaid health insurance plan, do not apply for VA medical care. As health care insurance increases over the entire country, the number of operating beds in the VA has actually fallen.

The members of the Puerto Rico Medical Association, as well as the general public, know that it is difficult for a patient to be admitted to the San Juan Veterans Hospital. My observation, from my own experience, is that a much higher proportion of the veteran population seeks medical care from the VA – irrespective of whether the veteran is service connected. In a single year, the number of hospital applications is so great that we must reject 70 percent of them.

In the rest of the United States, the rejection rate is 35 percent (3).

Because of this high rejection rate, the conclusion might be made that a second VA Hospital is needed. I shall have more to say on this matter later. For the present, please reflect on a few interesting facts, which are developed in Tables I-IV:

- The ratio of veterans to total population in the Antilles (one out of sixteen) is lower than in the total U. S. population (1:7);
- There are 5.5 beds per 1000 veterans in Puerto Rico, about 65 percent higher than in the fifty states;
- The annual per capita expenditure for veterans medical care at San Juan VA is \$130, compared with only \$80 in the VA system (4);
- There is a much higher ratio of veterans receiving outpatient care at San Juan than at the 201 other outpatient clinics operated by the V. A.;
- The rate of applications for hospital admission at San Juan far exceeds experience elsewhere.

With more than 90 percent of all Americans having some form of health care insurance, there is adequate explanation for the fact that many veterans can provide for their own medical care, particularly for short term illnesses and elective surgery. Repeated studies of VA hospital populations have shown that there is heavy emphasis on those with service related disabilities, plus non-service connected veterans who have limited incomes and/or protracted illnesses.

To the sophisticated readership of this Bulletin I need not develop the apparent reason for the heavy inpatient and outpatient demand at San Juan VAH.

TABLE V: REQUESTS FOR ADMISSION TO SAN JUAN VA HOSPITAL
COMPARED WITH NATIONAL EXPERIENCE

	All of United States	San Juan VA
Number of Applications in Fiscal Year 1972	1,440,000	37,000
Veteran Population	28,800,000	172,000
Number of Applications per 1000 Population	50	215

Source: U. S. Veterans Administration, VA Field Station Summary, June 1972, Part 3.

Veterans Administration Role in Health Manpower

Veterans Administration hospitals, clinics, and related facilities were originally established to provide medical care. Patient care continues to be their prime responsibility. However, the post World War II era has seen the development of important related functions in education and research. In 1945, VA's Central Office promulgated, with the assistance of leading medical educators, Policy Memorandum No. 2, which established affiliations with medical schools and other institutions of higher learning.

In the 25 years since Deans Committee affiliations were set up, VA has become increasingly involved in education and training of health manpower. It is estimated that 75 percent of all recent medical school graduates have spent part of their four years in a VAH and that 25 percent of all Board certified specialists acquired some or all of their experience in veterans institutions. As with physicians, many other members of the health team come to the VA for education or training — dentists, nurses, dietitians, psychologists, social workers, for example. Fifty five thousand trainees were in the VA last year, of whom 680 were at San Juan VA.

The VA role is not just to provide field experience. It goes much deeper. In many affiliations, the VA University relations are extremely close. At Birmingham, Alabama, the Staff of the VA and the Medical School are indistinguishable.

Veterans Administration Hospitals have been of great help to new, struggling institutions. Some years ago, when Seton Hall College of Medicine became the

New Jersey College of Medicine and Dentistry, it had inadequate facilities and space. The East Orange VA Hospital helped it over its difficult years by hiring staff and by providing space for medical school activities. Similarly the VA Center at Shreveport, Louisiana relinquished some of its space so that the new Shreveport branch of the Louisiana State University School of Medicine could start earlier than planned.

Some VA Hospitals have developed closed circuit television as a teaching device for both the VA and the affiliated institution — the VA installations at Wood, Wisconsin and Omaha, Nebraska are good examples.

In the final days of the 92nd. Congress, a Congressional resolution was enacted, and later signed by the President which emphasizes the national intent with respect to the future role of the VA. The resolution authorized the expenditure of VA funds during a five year period, to assist new and/or struggling schools of health professionals (5).

This new resolution is being enthusiastically received, and inquiries are coming to Washington from many states, even before the implementing instructions can be developed. It seems to me that this has important implications for Puerto Rico. In 1970, the Carnegie Commission made two proposals which relate to this matter; (a) It recommended the establishment of area health education centers in Ponce and Mayaguez; (b) It pointed out that VA resources could be called upon in selected situations (6).

Veterans Administration and Change

For those readers acquainted with the San Juan Veterans Hospital, but are unaware of other VA ins-

tallations, we ought to review what is going on here to illustrate what is new and different.

As an illustration, we in San Juan not only hospitalize veterans, but we also admit active service men. Although this occasionally occurs in the mainland, it is not a regular established custom. In the fifty states, active servicemen go to a military hospital. The different Puerto Rico situation has been dictated, of course, by the closure of Rodríguez Army Hospital.

A second illustration is the arrangement we have at San Juan VAH to provide dialysis for non-veterans. Until recently, the VA was prohibited from hospitalizing non-veterans except in life saving emergencies. However, Congress passed sharing legislation, Public Law 89-785, which authorized hospitals to make their resources and expertise available to the non-veteran community, provided veterans were able to receive necessary treatment first. Because San Juan's dialysis facilities were more than adequate for the treatment of veterans, VA's Central Office concurred in our suggestion that we cooperate with the Department of Health in arranging treatment of non-veterans.

There are many more possibilities for cooperation. For instance, the very successful renal transplant program headed by Dr. Thomas E. Starzl is a joint venture between Denver VAH and the University of Colorado. Cardiac surgery is a shared program between Palo Alto VAH and Stanford University School of Medicine.

The stimulus for sharing does not have to come from institutions of higher learning only. In some parts of the country, there are close working relationships with regional medical programs. In New England, plans are underway for the VA Hospital at West Roxbury, Massachusetts to change from its present role, paraplegic center for veterans, to a new role in which it treats all paraplegics, veterans or not, in New England.

Do these new ideas have application in Puerto Rico and the Virgin Islands? I certainly think so. Throughout the United States there is a demand for changes in the health care system. Depending on one's own view of the difficulty, his solution is one of the following:

- Build more medical and other professional schools, to counteract the manpower shortage;
- Stimulate the relocation of physicians, dentists, and others, so as to provide better coverage in rural areas;
- Encourage the growth of physician assistants and medical auxiliaries as a substitute for physicians;
- Provide either universal health insurance, or ca-

tastrophic health care coverage, to cover those major medical difficulties not taken care of in the usual insurance policy;

- Provide more medical treatment in outpatient clinics and in extended care facilities (e.g. skilled nurses home).

It is not VA policy to involve itself in the discussions on universal health insurance. Suffice it to say that the VA recognizes its clear cut requirement to provide medical care for eligible veterans, to assist the nation in solving problems in the health manpower field, and to make available its expertise in whatever fashion is appropriate.

Although all segments of the United States periodically request additional hospital beds, as has been suggested in Puerto Rico, the justification is sometimes weak. Although 125,000 hospital beds was the limit set in 1959, the VA is far below that figure thirteen years later. Medical and hospital practice have markedly altered hospital beds as a measure of activity. Many more veterans are now eligible for outpatient care. The need for psychiatric beds diminishes regularly. Nursing home beds and extended care facilities on the mainland have markedly lessened the demand for expensive acute VA hospital beds.

You might ask, what does all this mean as far as Puerto Rico is concerned? It has great significance, to my way of thinking.

I believe we can make better use of our 698 bed hospital if more opportunities can be found for extended care. We need to have available more suitable community nursing homes where veterans can be referred after acute hospitalization. We need to place more psychiatric veterans in foster homes.

I further believe that more veterans must have access to outpatient treatment nearer their homes. This year we shall disburse about \$500,000 to cooperating dentists who will treat veterans in their own communities, and another half million to physicians. VA's satellite clinics at St. Luke's Hospital and at Santo Asilo de Damas in Ponce are meeting an urgent need. If this new experiment begun July 1972, continues to be encouraging, our Central Office might be willing to embark on other such ventures.

The future of medical care in the Antilles, as well as in the mainland, is hard to predict. The Chief Medical Director, Dr. Marc J. Musser, expects that we shall have a pluralistic system, in which the VA will retain its identity, but will undergo great change. He has asked all Directors like myself to be prepared for such change, and to work with all interested parties.

San Juan VA and I stand ready to work with all of you in solving the difficulties which face us: Whether it is to establish a new medical school; to initiate special programs in surgical specialties; to set out in new directions in cancer research and treatment; or to use VA's rehabilitation potential for non-veterans.

Summary and Conclusions

1. The San Juan VA Hospital has a responsibility to treat service connected veterans, as well as those eligible non-service connected veterans who can be accommodated in our facilities.

2. Although medical care has been the traditional responsibility, in recent years veterans hospitals have become an important resource for training health professionals, and for providing specialized treatment for certain non-veterans through its sharing programs.

3. San Juan and its facilities are available to assist the entire medical community in its long range planning.

Enactment of universal health insurance will not hinder such VA cooperation.

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CEREBROVASCULAR AND PERIPHERAL VASCULAR DISEASE: PREVALENCE IN PUERTO RICAN MALES

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Vascular lesions affecting the central nervous system (International List 7th. Rev. codes 330-334) are the third most common cause of death in Puerto Rico. In 1970 death rates from this cause were 46.5 per 100,000 population, being somewhat higher in males (49.0) than in females (44.0) (1). Among males between 40 and 69 years of age the rate was 67.9 per 100,000 population. However, little information is available as to the prevalence and incidence of these diseases in the island.

Since 1965 an epidemiological study of coronary heart disease has been conducted by the University of Puerto Rico School of Medicine among 10,000 men residing in urban and rural areas. The initial findings in this study, which is still in progress, have been published elsewhere (2).

As part of the examination for the heart study an evaluation for cerebrovascular disease was performed. The presence of peripheral vascular disease, which frequently accompanies arteriosclerosis elsewhere in the body, was also evaluated. This paper presents data on the prevalence of these diseases in the population under study.

Materials and Methods

The population selected for study after a house to house census included approximately 12,000 men 45 to 64 years of age at the time of initial contact, who were residents of the urban areas of Bayamón, Guaynabo and Carolina and the rural areas of Naranjito, Comerío, Barranquitas and Corozal. Further pertinent details are presented elsewhere (2-10). Over 80 percent of subjects included responded for examination. A ratio of 2 urban to 1 rural male was part of the study design (2-3). At the time of interview subjects were questioned as to the sudden occurrence of muscle weakness, speech and visual defects. Duration and description of positive responses were obtained. Information on associated hospitalizations was obtained and pertinent hospital records abstracted. Questions on leg discom-

fort on walking were asked to ascertain the presence of intermittent claudication. The physical examination included evaluation of reflexes, cranial nerves, cerebellar signs, sensory deficit, localized muscle weakness, mental changes, and speech and visual defects. The extremities were examined for evidence of amputations, contralateral differences in skin temperature, and palpability of peripheral pulses. If abnormal findings were detected, Ratschow's postural change test for peripheral arterial insufficiency (11) was performed.

The diagnosis of cerebrovascular disease was made on the basis of: (1) evidence of focal brain disease, such as hemiplegia, monoplegia, aphasia, hemihypesthesia or sensory disturbance in the face, arm or leg, homonymous hemianopsia or monocular blindness, unilateral cerebellar ataxia, nystagmus, ocular or gaze paralysis, dysphagia or dysarthria, and (2) the temporal profile of the clinical syndrome. The temporal profiles used are as follows: (1) for intracerebral hemorrhage: grossly bloody cerebrospinal fluid, hypertension, rapid evolution over minutes or hours, onset during activity, rapid progression to coma, and headache (if patient sufficiently conscious to report what he feels); (2) for subarachnoid hemorrhage: sudden onset of severe headache, stiff neck, Kernig and Brudzinski signs, grossly bloody cerebrospinal fluid, absence of focal neurologic signs, a relatively transitory disturbance of consciousness, and subhyaloid (preretinal) hemorrhages; (3) for cerebral thrombosis: prodromal episodes, often with recovery or improvement between attacks, gradual evolution over a period of minutes to hours or longer, or saltatory progression, relative preservation of consciousness, clear cerebrospinal fluid, rapid improvement at times, constellations of symptoms and signs rarely seen with embolism, evidence of atherosclerosis elsewhere, and presence of disorders commonly associated with atherosclerosis; and (4) for cerebral embolism: sudden development of symptoms (within seconds or a few minutes), absence of prodromal manifestations, relative preservation of consciousness, clear cerebrospinal fluid, rapid improvement at times, focal neurologic signs or special arterial syndromes, a source of emboli, and evidence of recent embolism in other organs or in different cerebrovascular territories. Specific criteria designed beforehand for separation into definite and possible categories were applied, and the appropriate allocation was made by the majority of independent opinions of at least 3 physicians at special periodically scheduled review sessions held exclusively for the purpose (2-5).

Three criteria individually established a diagnosis of definite peripheral vascular disease: definite intermittent claudication, amputation due to a definite history of peripheral vascular disease as given by subject, or a positive Ratschow's test plus either difference in temperature of the feet or an absent pulse in the same leg. Possible peripheral vascular disease was diagnosed by three combinations of findings: (1) doubtful intermittent claudication plus either difference in temperature

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TABLE I: DEFINITE AND POSSIBLE CASES OF CEREBROVASCULAR DISEASES AND PERIPHERAL VASCULAR DISEASE AMONG 9,661 MEN AGED 40-69, BY AREA OF RESIDENCE (RATES / 10,000)

Disease	URBAN		RURAL		TOTAL	
	Definite	Possible	Definite	Possible	Definite	Possible
Embolie Cerebral Infarction	4.43	8.86	0	10.39	3.11	9.32
Atherosclerotic Cerebral Infarction	29.53	28.05	34.63	13.85	31.05	23.81
Intracerebral Hemorrhage	10.34	11.81	6.93	20.78	20.78	14.49
Subarachnoid Hemorrhage	2.95	5.91	0	13.85	2.07	8.28
Peripheral Disease	124.02	124.02	135.04	114.27	127.32	121.11
Total Population	6773		2888		9661	

of the feet or an absent pulse in the same leg, (2) doubtful Ratschow's test plus either difference in temperature of the feet or an absent pulse in the same leg, or (3) difference in skin temperature of the feet plus an absent pulse in the same leg as the colder foot. Criteria were applied by the physician at the time of the physical examination.

Results

Subjects with any of the four types of cerebrovascular disease and with peripheral vascular disease are shown in Table I by area of residence urban or rural, and separated into definite and possible categories. Because the numbers are so small no division by age groups has been attempted. The discrepancy between the figures for total population in the table, 9661 and those reported in previous publications, 9814, (2) is due to the omission of cases in whom the diagnosis was unknown because of an incomplete history or examination.

Taking into account the proportion of 2.35 urban to 1 rural subject in this sample, there seems to be no appreciable urban-rural difference in either cerebrovascular or peripheral vascular disease.

Discussion

This lack of urban-rural difference, although unusual, is not unexpected. No urban-rural difference in prevalence of coronary heart disease has been found in this sample in spite of sizable and significant urban-rural differences in many variables such as physical activity, body weight, ingestion of various nutrients, blood pres-

sure, heart rate, serum cholesterol and glycerides, blood glucose, and prevalence of hypertension and diabetes (2). On the other hand, the low numbers of prevalence cases may be accounted for by the high mortality that usually occurs in this illness. So, it is quite possible that larger urban-rural differences may exist and could be found among fatal cases. This information will be known at the completion of the second examination cycle, when incidence data become available.

Although there are no previous figures available for comparison, the over-all prevalence rate of peripheral vascular disease both definite and possible seems low at less than 3 percent, particularly in a sample of males of these age groups. The correlation of this disease with cerebrovascular disease or with coronary heart disease has not yet been determined in this study. If a high correlation is found, as is generally accepted, attrition due to mortality from the more severe illnesses may partially account for the low prevalence rate of peripheral vascular disease. Again this supposition will be verified or discarded when incidence data become available.

Summary

Very low prevalence of cerebrovascular disease and peripheral vascular disease was found among 9661 males 40-69 years old being followed prospectively mainly to ascertain reason for low coronary heart disease mortality rates in Puerto Rico. No urban-rural differences in prevalence were found, in spite of significant urban-rural

differences in behavioral, physical, electrocardiographic, dietary, and biochemical characteristics between these groups. Incidence data are necessary in order to determine how reliable are prevalence figures in assessing the problem of cerebrovascular and peripheral vascular disease in this group. They will also help to determine if the observed urban-rural differences in characteristics among men aged 40-69 are accompanied by urban-rural differences in cerebrovascular and peripheral vascular disease.

Resumen

Se encontró una prevalencia muy baja de las enfermedades cerebrovasculares y perifero vasculares en una muestra de 9661 varones entre las edades de 40 y 69 años participantes en un estudio epidemiológico que investiga principalmente las causas de las tasas de mortalidad bajas por cardiopatía arterioesclerótica en Puerto Rico. No se hallaron diferencias en la prevalencia entre los residentes de áreas urbanas y los de áreas rurales, a pesar de diferencias significativas urbano-rurales en características de conducta, físicas, electrocardiográficas, dietéticas y bioquímicas entre ambos grupos. Es preciso obtener datos sobre la incidencia de estas enfermedades para poder determinar cuán confiables son las tasas de prevalencia en la valoración del problema que presentan estas enfermedades en el grupo bajo estudio. También permitirán establecer si las diferencias urbano-rurales observadas en las características de los varones de 40 a 69 años de edad se acompañan de diferencias urbano-rurales en enfermedades cerebrovasculares y perifero vasculares.

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A NATIONAL HEALTH PROGRAM (*A View of Some Other Experiences as They Relate to our Future*)

George A. Silver, MD

The impatience of the consumer of medical care is becoming increasingly evident. Poor people have difficulty in obtaining medical services; the middle class is irritated with steeply rising costs and diminishing availability; the better educated complaint of these matters and of poor quality and bad service as well.

It is true that some or all of these complaints have been heard in the USA for at least 50 years. We have had a report to the American Medical Association as far back as 1916 urging compulsory health insurance to cure some of the ills. And in 1928 there was the Committee on the Costs of Medical Care, in 1939 the Wagner-Murray-Dingell Bill. In 1949 there was the President's Committee on the Health Needs of the Nation, in 1966 the National Commission on Health Manpower. Most solutions are as familiar as the earliest ones:

- Insurance to reduce the impact of unanticipated cost;
- Prepayment to prevent inflation and reduce economic obstacles to access;
- Reorganization via group practice or Health Maintenance Organization as now popularly designated;
- Systematic correction of various elements, outpatient care, inpatient care, long term care;
- Regionalization to reduce duplication and waste, introduce more efficient use.

At every juncture, the objections raised were equally familiar:

- Inadequate manpower;
- Maldistribution of manpower;
- Threats to quality through bureaucratization;
- Loss of incentive to efficiency and quality.

Of course there were those who denied there was a problem and insisted the system as currently organized and financed worked well enough. They prophesied ominous results from tampering with the system.

Over this 50-year period, it became more and more apparent that the defects in the system (which even its

proponents admitted!) were growing worse and less tolerable. Furthermore, social change and growing rebelliousness against social injustice intensified the discontent and magnified the deficiencies. In 1928, maternal mortality in non-whites was twice the maternal mortality in white women. By 1968 the overall maternal mortality had declined steeply for both whites and non-whites. But not at the same rate, for now non-white maternal mortality was 4 times the white! The society of 1928 which could tolerate 60 deaths per 10,000 live births in white mothers, (120 in non-whites) now refused to tolerate 10 deaths per 10,000 live births in non-white mothers, 2.5 in whites.

Physicians had rearranged themselves, too. There were no fewer doctors per 1000 population in 1970 than in 1928. But most of the doctors were specialists in 1970 and most had been general practitioners in 1928. A "primary care" physician was much harder to come by in 1970 than he had been in 1928. Furthermore the younger doctors as they had come into practice shunned the countryside and the ghetto areas of the cities and settled in prosperous suburbs and around teaching hospitals.

While Los Angeles, for example, had 127 physicians per hundred thousand population, in the southeast district of Watts there were only 38. The fifty thousand people who live in the impoverished Kenwood-Oakland area of Chicago are served by a total of 5 physicians in their community. In addition the county hospital and clinics are 8 miles away. In Baltimore there are only one hundred general practitioners for 550,000 people living in the slums, and all but ten of them are at least sixty years old.

If we want to look at specialty distribution, state variations alone are vast. The District of Columbia has an internist (who so identify themselves in American Medical Association records) for every 1200 people. Mississippi has one for every 12,000. New York has a pediatrician for every 6800 people. Mississippi has a pediatrician for every 24,000. Nebraska has an obstetrician for every 1270 people, but Mississippi has one obstetrician for every 18,600 people.

What about Puerto Rico in these evaluations? Well,

From the Department of Health, Yale University. Delivered to the Puerto Rico Medical Association, San Juan, November 16, 1972.

Puerto Rico has an internist for every 7700 people - about half the average for the United States, where there is one to every 4400. Puerto Rico has a pediatrician for every 12,000 population, which is average for the United States; and Puerto Rico has an obstetrician for every 15,000 people, which is not quite so good as the rest of the United States which has one for every 12,000. Of course, when it comes to general surgery the situation is quite different, for there we find that while the national average is one surgeon for every 7500 people and New York has the most, one to 4800, Puerto Rico has the fewest - one to 14,700.

There is indeed a difference in the distribution of physicians.

In addition, the complexity of new inventions and discoveries, technological advance, created the need for new machinery for diagnosis and treatment requiring new hands. There are 3 million health workers now and they too are short when doctors are short, because they are tied to hospital and medical practice.

So the poor and the minorities and rural people get short shrift, while our society cries for equity. The pressures for change in the medical care system are consequently enormous. Fifteen or more bills were before the 92nd Congress for more or less radical reform of the organization and/or financing of the medical care system. These were by no means partisan efforts, either. Both parties took part in the legislative jockeying. Perhaps because of this, that there were partisan interests at stake, very little was accomplished this time. But in the next Congress?

At this point I think it is fair to say that the most vigorous opponents of any change, among physicians, have reconciled themselves to *some* change and will perhaps cooperate in any new system, if only to a limited degree. In other words, the doctors are ready for *something*.

In a new book "U. S. Health Care: What's Wrong and What's Right" by Stephen Strickland, some interesting data on doctors' attitudes are revealed. For instance, 51 percent of doctors favor some legislation for a national health insurance program (59 percent of those in specialty practice).

And as for patients, 61 percent believe basic changes are required in making medical services available. So, the patients are ready for change, too.

In a word, the USA is at the threshold of significant change in the organization and financing of medical care and perhaps in the delivery of services as well. Maybe I am too sanguine about the possibility and you should know that I have a bad track record. I have been thinking we are on the threshold of change for over 30 years!

My good friend, Dr. Thomas McKeown, Professor of Social Medicine at Birmingham in England, once wrote (25 years ago!) about the possibility of the USA legislating a National Health Service, that, "both parties practice a form of political contraception in which no matter how suggestive the preliminary movements, there are no embarrassing legislative consequences".

What may we look forward to?

I would like to examine this question from two different standpoints. On the one hand, I'd like to review with you some of the developments in other countries and on the other relate these facts to the kinds of legislation proposed for the USA in the last Congress.

Looking ahead, we should look North first. The Canadians have had, for almost 10 years, their own brand of Medicare. Under that system, each province has developed its own plan, with substantial financial support from the Federal government. Each person is covered for outpatient, in-patient, long term care and associated costs. With the exception of those doctors who are working in prepaid group practices (a minority of doctors) the physicians are paid on a fee-for-service system. Each province varies the system a little, but basically the whole country has health insurance. Patients see their doctors, are hospitalized as before and the doctors are reimbursed through third parties. Very little has changed except for that latter point. Inflation is plaguing their system, much as it plagues ours, though not to the same degree. After some brief flurries of discontent, the doctors seem to be reconciled. Much is as before.

What about Britain? One hears of radical reorganization imminent - by 1974 to be precise. Isn't this evidence that the system is in trouble? Maybe the famed British National Health Service isn't working and they'll return to fee-for-service, entrepreneurial practice? Hardly likely.

Britain is going through the throes of change to a higher stage of organization, not dismantling of their plan. Having learned that too highly centralized operations lead to inertia, they are decentralizing the services on new geographic lines. Having seen that separation of general practice and ambulatory care on the other hand from specialized practice and inpatient care on the other leads to inefficiency and professional dissatisfaction, they are unifying the system. Recognizing that community health planning and health program evaluation are the latter day equivalents of the sanitary revolution, they are moving to convert the health officers into community medicine specialists.

After 25 years, general practitioners will be given in-

centives to practice in groups instead of solo practice, to be associated with hospitals and to undertake home care programs.

Otherwise, patients will get care substantially as before: they will go to their doctor's office, he will send them to the hospital if they need that care.

Doctors will be paid as before. General practitioners by capitation, specialists by session or salary. The bulk of the money will come from general revenues, income taxes. Again, the mixture very much as before.

In Sweden, a recent reimbursement reform fixes the doctor's fee for a service. But he is still paid fee-for-service and his patient still seeks him out in the traditional way. As before.

I could go on to Denmark, France, Belgium, Holland, where there is current ferment and discussion about the medical care system. But the source of the ferment and discussion lies in the ominous inflation of medical care costs and the efforts are directed mainly at control of these inflated costs, not at the method of practice. All over, the matter of medical practice is very much as it was.

Given all that, what can we say about the future organization of medical practice in the USA? Even under the most radical of bills, I suspect that except for the reimbursement mechanism, the mixture will be very much as before. Our democratic legislative processes tend to be slow and cautious. We talk about change for a long time, recognize its desirability, agree to accept it, but don't legislate it for ever longer, and when we do, it is generally less than most people are already prepared for.

The bills proposed up to now, range from the President's plan to a comprehensive prepaid Federally operated program. The President's plan, a family health insurance plan, is an insurance plan to replace Medicaid and contains a cost-sharing element, so that many families eligible for insurance will have to pay some part of the cost. In addition it provides for employer-employee contribution to private health insurance plans. An even less inclusive proposal provides for completely voluntary health insurance in which employees and employers could elect coverage, or individuals elect to join a health insurance plan, and the State provide a plan similar to the Family Health Insurance Plan, but under their own auspices and through private insurance companies. These are the minimal programs proposed. The Javits bill extends Medicare over time to the whole population. Senators Scott and Percy propose that inpatient or hospital care only should become a compulsory federal program financed by payroll taxes and general revenues,

while outpatient care would continue to be covered in the voluntary fashion and through private insurance with the government subsidizing premiums for low income families. The Kennedy bill, cosponsored by a great many Congressmen and Senators and based on the original bill introduced by Congresswoman Griffiths, provides for a comprehensive national health insurance program with a Federal health board, regional operating offices, funded by way of a combination of payroll tax and general revenues, with everyone eligible for hospital, physician office and home visits, prescription drugs for chronic and other specified illness, and so forth, including nursing home care. The American Medical Association was represented by a number of bills: The Fisher bill allowed for credits against personal income taxes to offset the premium of voluntary health insurance. The Fulton-Broyhill bill, which was explicitly endorsed by the American Medical Association, provided for credits against income tax to offset premiums in health insurance. It differed from the Fisher bill only in minor details. Both bills provide for sharing of costs, a coinsurance element, and catastrophic coverage, with a corridor deductible and out-of-pocket payment varying according to income and additional costs of hospital days covered.

The range is clearly very great among these bills as to how the insurance shall be paid for, who shall be eligible, what shall be covered.

Yet with all these, present methods of practice are possible and in all likelihood will continue. True, there are incentives for adopting new modes and the implications that if doctors adopt these new methods of practice, gratifying income augmentation will result. Until the evidence is unmistakeable, most doctors will wait and see.

What about the Health Maintenance Organization? There will undoubtedly be Health Maintenance Organization legislation — the President asked for it, Senator Kennedy wrote the bill. Everyone wanted it. But was it just the jam and back log of congressional action that prevented its accomplishment this year? I believe not. The Health Maintenance Organization is basically prepaid group practice and there are proponents of improved system organization in medical care who don't believe group practice is necessarily the way. They point to the Medical Service Foundation experience, to that of the Windor Medical plan with many years of successful operations and they want a Health Maintenance Organization bill that sanctions much broader system management than group practice alone. The Kennedy bill in the Senate and the Rogers bill in the

House will have to be adjusted before there will be Health Maintenance Organization legislation.

And when there is Health Maintenance Organization legislation, it is clear that there will be progress in including larger numbers of people only if there will be associated national health insurance to pay for it. The Health Maintenance Organization itself needs the fuel of insurance support to run. So, in the long run, we might say it will not be the Health Maintenance Organization legislation that will precipitate change, but the financing legislation, whatever it may be.

Other, far less persuasive solutions have been urged on us and may even become law. We are assured that the critical manpower situation, the critical shortages in doctors, nurses and technicians must be resolved and being resolved will make all the other changes possible. I don't see that as the panacea, either. While the shortages and maldistribution of personnel are grave and obstruct easy solution of our medical care problems, these shortages and maldistribution will not easily be resolved by turning out more trained people. There is reason to believe that more people will only make it possible for the people now getting care to get more care.

I would like to introduce, at this point, a related consideration with regard to the health manpower situation, that has to do with the lack of representation of minorities in the health professions in adequate numbers. While it may not be true that increase in numbers will solve the problem, it could very well be that some part of the problem, that is, attention to the needs of the disadvantaged, of the minority, of the slum-dwellers, would be better met if health professionals were drawn from those strata of the population. The shortage of health care personnel from among minority groups is huge. While minorities are 15 percent of the population, less than 5 percent of all professional health workers come from these groups. The higher the professional level, the lower the minority representation. Sixty percent of licensed practical nurses are non-white, for example, but only 2 percent of physicians are non-white. Most medical schools are just beginning to admit minority students for the first time. It is true that so little orientation and stimulation of minority group students for application to other kinds of health science schools has been provided, so that many of the other schools can virtuously respond that they do not have blacks or Chicanos or Puerto Ricans because they do not have "qualified applicants". This is a matter that is being rapidly remedied, as organizations like the Health Manpower Development Corporation move to

create community and professional groups to stimulate young people from among the minorities to recognize the opportunities in the health professions and to equip themselves to create larger and larger pools of applicants.

While the situation will not be resolved, it will certainly be improved, when larger numbers of minorities are represented in the health professions.

So long as health insurance is biased in favor of inpatient care, as it now is, and people can buy pretty much what they choose or can afford, producing more trained professionals may not mean better distribution of specialists either. There is nothing that guarantees that the increment will become the primary care physicians we need, and not more surgeons. Or that they will practice in areas now critically short, and not in the suburbs.

No, simply more people produced won't solve our problem.

Well, what about rationalizing the system so that trained people do only what they are trained for, and not added tasks requiring less sophisticated skills? Can't we train lots more people at lower skill levels and assign tasks hierarchically?

Yes, we can, but without a highly organized system into which these added people would fit, what's to keep the same over use and misuse of care to occur that was mentioned above? And if we are to have a tightly structured system, how will we get past the legislative barrier? This is not to mention the added problems introduced by the new types of workers: Will they be uniformly licensed in all States? Will they have any upward or lateral mobility? Can they become doctors or nurses, in other words, through credit for proficiency as well as academic credit? And how are they to be paid and what is to prevent their being exploited? These are very serious questions for a group of professions rapidly becoming unionized.

I will spend very little time in discussing another popular solution to the health care crisis: multiphasic screening and preventive medical services generally. Not to respect the value of prevention is to avow the blackest heresy and I will not do it. But I must raise serious question about what we know that we can prevent, what we have to do to discover disease early or in advance of its manifestations and how frequently the test for discovery must be made in order to make any inroads on disease. These are hard questions and there are many years of experimentation yet to be done before even partial answers are available.

As for multiphasic screening, without a medical care system to back it up, what good is it? No, for some

time to come, until we can rescue people from self poisoning with tobacco, alcohol, drugs, automobiles and pollution generally; and until we know what diseases can be aborted; and until there is a system for catching the reported patient and treating him, I am skeptical of the solutions of "technology".

What have we then? Well, we have, for the foreseeable future, very much more of the same, with a strong likelihood that there will be a health insurance law that takes away the burden of payment at the point of illness and use, but not much more. I'm afraid it isn't going to be enough. And I'm afraid it will continue and maybe even exaggerate some of the difficulties it is intended to offset.

I'm afraid poor people will still have difficulties in finding and obtaining medical care. Quality may improve, with supervision, peer review and the like. But access will still be difficult for rural people, minority groups, ghetto dwellers. Redistribution of personnel, in other words, will not automatically take place.

I'm afraid there will still be inflation, if there is fee-for-service as the model of reimbursement.

In this instance, perhaps I'm too pessimistic! Well, I explained earlier about my poor track record as a prophet. Yet as I look at the future, I see the major need as essentially a revamping of social priorities, not a trendy tinkering with the medical care system. The problem is essentially *equity*. The problem is not economic or technological. If we want everyone to have equal access to medical care services, because it is common humanity we share that demands it, we

can do it.

Of course, some of us will have to wait in line, to which we are not accustomed, income level having no influence on professional interpretation of priority of need. When I served in the shock ward of a field hospital on the battlefields of World War II, my charge was to classify patients by the urgency of need for surgery there, not by their rank.

In such a revolution of social sentiment, doctors and other professional workers will gladly undertake to re-establish themselves in disadvantaged areas and redistribute resources as required. Medical schools and other professional training institutions will stretch their capacity to turn out the additional personnel required. The teachers will work longer hours, much more than 5 days a week and forego trips to meetings in Puerto Rico and Europe in order to multiply the classroom teaching and clinic exercises.

However, this decision is a social decision, like reducing air and water pollution, or withdrawing useless and dangerous drugs from the market, or building housing for slum dwellers. These are not decisions that can be forced on society. They are decisions society must make for itself.

They may not be popular, or acceptable, decisions, but they ought to be discussed. The grievances will not be redressed unless we want them redressed. "The times cry out for change", said Mr. Gardner, "and our institutions resist change with unholy stubbornness".

There will be no equity in medical services unless we the people want equity.

EL TRASPLANTE DE RIÑÓN EN EL TRATAMIENTO DE LA INSUFICIENCIA RENAL IRREVERSIBLE

E. A. Santiago Delpín, MD

La insuficiencia renal terminal, y su consecuente síndrome urémico careció de tratamiento efectivo hasta la década de los '40, cuando Kolff en Holanda, y luego Alwall en Suecia desarrollaron un riñón artificial de aplicación clínica. No fue hasta el 1960, cuando Quinton y Scribner introdujeron una cánula vascular de implantación permanente, que se utilizó este tratamiento en pacientes con fallo renal crónico; subsiguientemente, nuevas cánulas y técnicas de acceso a la circulación permitieron el uso rutinario de estos métodos.

Otros también abordaron el problema con un punto de vista diferente. Razonaron que un riñón ajeno podría depurar la sangre del enfermo. Aunque intentos esporádicos e infructuosos ocurrieron desde 1902, fue Lawler en 1950 quien implantó por primera vez un riñón de cadáver a una paciente con insuficiencia renal terminal. La intervención exitosa resultó en cinco años de vida activa y productiva. Otros investigadores intentaron experimentos similares con éxito temporero.

Ante la disparidad genética, Murray utilizó un donante gemelo en 1954; al obtener función prolongada y sin rechazo comprobó que el obstáculo principal para el éxito de los trasplantes es la barrera inmunológica.

Indicaciones Quirúrgicas y Selección del Paciente

Al principio se establecieron criterios rígidos para seleccionar candidatos para trasplante y diálisis. Al acumular experiencia, estos criterios fueron modificados. Actualmente, la indicación principal es la insuficiencia renal severa e irreversible. Las contraindicaciones principales son el cáncer generalizado y la sepsis descontrolada. Enfermedades crónicas tales como diabetes, úlcera péptica, tracto urinario anormal, arteriosclerosis, síncosis, y lupus, previamente contraindicaciones absolutas, se consideran hoy como sólo relativas, y la selección en estos casos se individualiza.

Niños, desde recién nacidos hasta tres meses de edad, han pasado por diálisis y trasplante con éxito; con resultados adecuados y aún mejores que en adultos. También, pacientes hasta de 80 años han tenido trasplantes. Sin embargo, la selección en este grupo debe ser más cuidadosa, ya que los resultados no son óptimos, especialmente con el donante cadáver.

El "candidato ideal" lo constituye el paciente joven, con insuficiencia irreversible, sin otra enfermedad, y estable psicológicamente.

Seleccionado el paciente, se prefiere comenzar el tratamiento cuanto antes porque las complicaciones de la uremia prolongada pueden deteriorar su condición general. Los adelantos recientes en diagnóstico renal y diálisis permiten esta decisión con más certeza y premura.

El Donante

El Donante Vivo:

Consideraciones médicas, morales y legales entran en la decisión de utilizar un donante vivo. Todos los centros de trasplantes del mundo exigen la perfecta salud del donante, a quien someten a una rigurosa evaluación, que incluye un historial detallado, examen físico, examen psicológico y sociológico, evaluación renal y cardíaca extensa, aortograma y tipificación inmunológica contra el recipiente. Por supuesto, se enfatiza el elemento voluntario de la donación. Un 33 por ciento de los pacientes así evaluados son rechazados al descubrir condiciones médicas que contraindican la donación.

En 3,000 trasplantes de donante vivos en el mundo, una sola muerte ha ocurrido posiblemente relacionada con la donación. Tras larga evolución y valoraciones repetidas, se estima que la supervivencia a 20 años en pacientes con un solo riñón, es tan sólo 0.2 por ciento menor que la de la población normal, el peligro de muerte a corto y a largo plazo es mínimo, y probablemente insignificante.

La morbilidad operatoria es la esperada para cualquier operación de magnitud similar, y consiste de complicaciones pulmonares, urinarias e incisionales. No obstante, la nefrectomía en el donante vivo, es proba-

blemente la única operación que representa riesgos definitivos, sin derivar beneficio físico alguno. Sin embargo, los beneficios psicológicos en el donante son la regla. Seguimos estimulando la donación viva, ya que los resultados obtenidos son superiores a aquellos de donaciones de cadáver. Una vez perfeccionadas las pruebas de histocompatibilidad y los métodos de inmunosupresión, y con mejoría en los resultados obtenidos con el donante cadáver, el uso de donantes vivos, será abandonado. Quizás se llegue a utilizar el xenotrasplante de otras especies, aunque actualmente, esta modalidad no ha tenido éxito clínico.

El Donante Cadáver:

Durante los últimos años, se ha desarrollado el concepto de "muerte cerebral", basado en parámetros neurológicos y neuro-electrofisiológicos, concepto aceptado por la comunidad legal, médica y laica. El diagnóstico de muerte cerebral lo hace usualmente un grupo independiente, compuesto de neuro-cirujanos y/o neurólogos.

La autorización del familiar más cercano es necesaria, aunque en Estados Unidos la mayoría de los estados ya aceptan la "Ley Universal de Donación de Organos", la cual permite a una persona el donar sus órganos en vida, sin necesidad de obtener permiso familiar.

Dos consideraciones adicionales son de importancia en la selección del cadáver donante. Este debe estar libre de infecciones y de cáncer transmisible al recipiente, excluyendo cáncer cerebral o dermal. Además debe existir evidencia reciente de función renal normal, aún cuando el deterioro pre-terminal altere las funciones en grado leve.

Histocompatibilidad

Definimos este término como la presencia o ausencia de antígenos específicos en o dentro de las células, los cuales determinan el desarrollo de anticuerpos en el recipiente, y en consecuencia el rechazo del órgano trasplantado. Compatibilidad sanguínea es el primer requisito, de modo que el recipiente no tenga isohemaglutininas en su sangre contra la del donante. Aparentemente, los antígenos mayores (ABO) están representados en cantidades significativas en otros órganos, mientras que los menores, y el factor Rh no aparecen tener importancia práctica alguna.

Varias técnicas pueden identificar las diferencias antigénicas entre el donante y recipiente. De éstas, la principal es la tipificación de tejidos. El cultivo mixto de linfocitos sirve para corroborar algunos casos. Con estas pruebas se intenta lograr mayor seme-

janza entre el par antigénico. La tipificación de tejidos consiste en exponer los linfocitos del paciente y del donante a un panel de antisueros específicos. La destrucción de los linfocitos por algunos sueros definen su "tipo". Al comparar el tipo del recipiente con el de su donante tenemos una idea de la semejanza inmunológica entre ambos. En el cultivo mixto de linfocitos se mezclan los linfocitos del paciente y su donante en un medio de cultivo artificial. Diferencias antigénicas se manifiestan por transformación blastogénica de los linfocitos, la cual se mide por el consumo de timidina radioactiva.

Un punto esencial es el utilizar pruebas de linfotoxicidad para demostrar anticuerpos preformados en el recipiente. Esta situación suele encontrarse después de transfusiones múltiples, durante diálisis. Como consecuencia el paciente desarrolla anticuerpos contra los antígenos de leucocitos, y por ende de otros órganos. El trasplante está contraindicado en ese momento, ya que el riesgo de rechazo es muy alto.

Técnica Operatoria

Se implanta el riñón en la fosa iliaca del recipiente. La circulación se restablece por medio de anastomosis de la arteria y vena del órgano donado, a la arteria hipogástrica y la vena iliaca común del recipiente. El uréter usualmente se implanta en la pared posterior de la vejiga, a modo de neoureterocistostomía. Durante la nefrectomía del donante, se pone particular cuidado en manipular el riñón con delicadeza, ya que el espasmo vascular es frecuente y lleva a complicaciones de fallo renal agudo post-operatorio. Por igual razón se intenta inducir una diuresis constante y casi exagerada durante la operación.

En el caso del donante cadáver se pueden remover los riñones individualmente, o ambos en bloque con la aorta y vena cava. Esta última técnica ha probado ser muy útil cuando paro cardíaco inesperado hace necesaria una disección rápida, o cuando se obtienen riñones de cadáver infantil o recién nacido, en cuyo caso se utiliza la aorta y cava del donante para las anastomosis. En la mayoría de los casos, estos órganos deberán preservarse mientras se preparan recipientes. A tal efecto, se preservan en sistemas especiales que incorporan perfusión con plasma humana, enfriada y oxigenada, y que pueden mantener un riñón en estado viable por casi tres días.

Factores en el Manejo del Paciente con Trasplante

Los siguientes factores son importantes en mejorar

la sobrevida del paciente trasplantado:

1. El tratamiento más temprano.
2. La hemodiálisis prepratoriaa antes del trasplante.
3. La eliminación de todo foco infeccioso antes de la operación.
4. Remover los riñones enfermos en una operación preliminar separada, algunas semanas antes del trasplante.
5. El énfasis en la protección del riñón durante la nefrectomía del donante.
6. El énfasis en el cuidado durante la implantación del uréter, evitando complicaciones urológicas.
7. El uso cuidadoso de los inmunosupresores, evitando las complicaciones de neutropenia e infección.
8. El manejo intenso del paciente en la clínica, identificado y tratando los problemas temprano.

Inmunosupresión

La irradiación corporal para producir inmunosupresión se utilizó por primera vez en Boston, en 1958. Las complicaciones de la radiación fueron muy serias, y aparte de algunos grupos esporádicos, se abandonó como tratamiento principal. Sin embargo, la radiación local al órgano aún se usa, bien sea durante el trasplante, o en episodios de rechazo.

Murray fue el primero en usar azotiaprina (Imuran) en el trasplante clínico. Más adelante se encontró que la combinación de azotiaprina con esteroides, tenían un efecto inmunosupresor aditivo. Finalmente, el suero antilinfocítico (ALG) fue introducido pro Starzl para uso clínico. El régimen combinado de "Azotiaprina-Esteroides-ALG-Radioterapia local" en varias dosis y combinaciones, parece ser el más confiable con que contamos hoy día para inmunosupresión profiláctica y control del rechazo.

La timectomía, el drenaje de linfocitos y la erradicación extracorpórea de la sangre han tenido resultados variables. La búsqueda de sustancias que modifiquen el antígeno sin alterar las defensas del recipiente, es una de las áreas de investigación más intensa que existen hoy día.

Resultados

El noveno informe del Registro Nacional de Trasplantes nos demuestra la mejoría en los resultados alrededor del mundo. Asumiendo condiciones adecuadas se puede esperar una sobrevida de un año, en trasplantes entre hermanos, de 80-87 por ciento,

en trasplantes de padre a hijo, de 70-75 por ciento, y en trasplante de cadáver, de 50-65 por ciento.

Estas cifras disminuirán algo en años subsiguientes. Durante los próximos 3-4 años se espera acumular data de aquellos pacientes manejados con los métodos descritos, y se podrá determinar la sobrevida a cinco años. No obstante estas cifras ilustran el progreso alcanzado con el trasplante de riñón en años recientes.

Rehabilitación

El paciente trasplantado tiene que seguir un riguroso régimen de medicamentos y evaluaciones periódicas. En cambio, puede llevar, como lleva la mayoría, una vida relativamente libre. La restricción de dieta y líquidos no es severa, y la sensación de bienestar es notable. El precio de esta mejoría es el seguimiento intenso, y los cambios físicos que resultan de la administración prolongada de esteroides. Esto, por supuesto, es más marcado en el paciente con riñón de cadáver, ya que las dosis requeridas de prednisona son mayores. En el recipiente de donante vivo familiar, las dosis son más bajas y los cambios son usualmente mínimos.

Conclusión

La hemodiálisis y el trasplante han atacado el problema de la insuficiencia renal irreversible desde dos puntos de vista distintos, y ambos han logrado un éxito satisfactorio. Estas modalidades son interdependientes y se necesitan entre sí. Centros puros de trasplantes o de hemodiálisis no son prácticos ni adecuados. Por tanto el concepto de "centros de tratamiento renal", donde ambas disciplinas trabajan conjuntamente, ha ganado aceptación.

El trasplante de riñón, ha llegado por lo menos a su adolescencia. Se ha perfeccionado la técnica quirúrgica; se han controlado las complicaciones operatorias, urémicas e infecciosas; la barrera inmunológica ha sido definida y controlada parcialmente. Nos resta ahora, descubrir métodos más específicos y con menos efectos secundarios indeseables para modificarla y eventualmente vencerla.

Agradecimiento

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Bibliografía completa de este artículo podrá ser obtenida a través del autor en el Departamento de Cirugía, Recinto de Ciencias Médicas, Universidad de Puerto Rico, San Juan, Puerto Rico.

ASPECTOS MEDICO-LEGALES

SALE OR DISPOSITION OF A MEDICAL PRACTICE

(Prepared by The Office of the General Counsel of the American Medical Association)

INTRODUCTION

The purpose of this article is to offer some practical suggestions on the sale or disposition of a physician's medical practice. It is hoped that this article will assist the physician in planning for his retirement, but more importantly, it is hoped that this article will alert the physician to the importance of providing the means and direction to enable his family to dispose of his practice in the event of his death. The consideration which the physician gives now to the disposition of his practice will be beneficial in many ways to those members of his family who may face that task at a later time.

PARTNERSHIP AND CORPORATE PRACTICE

The physician who practices in a partnership or a corporation (many states, by special legislation, now permit physicians to form a corporation for the practice of medicine) may have entered into an agreement with his partners or his fellow shareholders which provides that upon the death of any member of the group, the surviving partners or the corporation must purchase the interest of the deceased physician. Frequently, this arrangement is funded by the required purchase of life insurance on each partner or shareholder, so that the money will be available upon the death of any partner or shareholder to purchase their interest in the partnership or corporation. The proceeds of the life insurance may be payable to the corporation, the individual partners, the partnership, or a third party (trustee), and then paid to the estate of the deceased physician in return for his interest in the partnership or corporation. In this type of arrangement, which lawyers frequently refer to as a "Buy and Sell" agreement, the amount to be paid for the deceased physician's interest is determined by a formula which has been agreed to by all of the partners or shareholders. This relieves the family and the other partners of the unpleasant task of negotiating the purchase price. If properly drawn and fully understood by the physician at the time he enters into this agreement, it should in all events be an equitable disposition of the practice for both buyers and sellers. Like a Will, it should be drawn by a lawyer, upon lawyer's advice, and should be reviewed periodically by the parties and their lawyer for possible revisions resulting from changed circumstances or new tax consequences.

The physician who practices in a partnership or a corporation which does not have a "Buy and Sell" agreement for its members will encounter many of the same problems as the sole practitioner, when it comes time to sell or dispose of his practice. The following chapters, therefore, will be of interest to all physicians, no matter what form their practice takes.

PHYSICAL ASSETS

The most obvious assets of a physician's practice offered

for sale are the fixtures, equipment, supplies, perhaps an office lease, and the goodwill of his practice. The first principle which is perhaps too obvious to require special mention is that the sale of the entire practice is normally more desirable to the seller than a piecemeal sale, which may eliminate the value of the goodwill.

The physician who maintains his office in his residence, and the physician who owns the land and building in which his office is located, separate from his residence, present specific problems which can only be adequately resolved by consultation with the physician's family lawyer. Depending upon the plans of the retiring doctor or the wishes of the deceased physician's family, a plan will have to be tailored by the attorney to accomplish the best result, having due regard for cash needs and tax consequences.

In any sale, the fixtures and equipment would include equipment used by the physician directly in the practice of medicine. In any sale of such fixtures and equipment there should be an allocation of a sale price to each particular item rather than grouping all fixtures and equipment together for a single price. This is because of the necessity for determining the tax base of each item for income tax purposes. There are two rules for determining the tax base, depending upon whether the sale is being made by the owner of the equipment, or by the estate of a deceased owner. The rules are as follows. The tax base of each item of fixtures or equipment is the fair market value at the date of death if the sale is being made by the estate of a deceased owner, but it is the purchase price less accumulated depreciation if the sale is being made by the owner of the equipment. The amount by which the sale price exceeds the tax base constitutes a capital gain for tax purposes and conversely, the amount by which the tax base exceeds the sale price constitutes a capital loss. The relationship of the sale price to actual open market value may be somewhat strained, but due regard should be had for the tax consequences of the sale. The sale price for the fixtures and equipment should not be finally determined until all other phases of the sale have been considered.

In the event that either the fixtures, equipment or supplies have not as yet been paid for in full, there may be a mortgage or security lien recorded against the ownership of such property. Of course a release of any such lien must be obtained at the time of sale so that the purchaser can acquire a clear unencumbered ownership of the property. It is customary to use the proceeds of the sale to liquidate any indebtedness remaining on the items of property being sold. This is especially true if the purchaser is financing the acquisition. In such case, the buyer's lender will normally handle the necessary mechanics to obtain the release of the seller's existing mortgage lien. However, the seller also has a significant interest in making certain that any lien is paid in full before the equipment is delivered to the purchaser. If the buyer does not pay the lien, the seller remains liable for any amount still due. Therefore, the seller should require adequate evidence of the payment and release of any lien which is deducted from the purchase price. *(Will continue)*

EDITORIAL

POLLITO, CHICKEN; GALLINA, HEN; PLUMA, PENCIL Y LAPIZ, PEN

Al iniciarse un nuevo año, como en los anteriores, me parece propicio llevar a los lectores del Boletín alguna que otra observación, algunos comentarios personales. No por anunciarse más calmado que el que deja atrás, será el 1973 una excepción.

*Nuestro título traspone algunas palabras. No fue precisamente así como se nos enseñó ese versecito en los grados primarios. Allí, tendidos sobre alfombritas se nos instruyó correctamente durante los ratos de descanso, y la mayoría de las veces lápiz fue **pencil**, y pluma, **pen**.*

*Los errores surgieron después. Ninguno se remonta a la infancia, ni siquiera a la juventud Entonces, lápiz se convirtió en **pen**, a veces, otras era **pencil**, en alguna ocasión lápiz, y de cuando en cuando también era otras cosas, según conviniera.*

Pollito, "chicken": No abundaré sobre el uso, desuso o maluso de uno u otro idioma, o de ambos, en la medicina de Puerto Rico. De opinar, en forma diversa, se han encargado ya algunos de nuestros colaboradores. Nos escribirán, oiremos de otros pareceres, y serán bienvenidos. Aquí el lector tiene puertas abiertas.

Solamente deseo referirme a la costumbre, dominante en muchos hospitales, de que los médicos redacten sus expedientes clínicos en inglés. Luego de pasar doce años en Estados Unidos, y un par más en Puerto Rico, haciendo lo mismo, me convertí al español. La fe me llegó de pronto, como a San Pablo que se cayó del caballo y quedó ciego varios días (así fue de traumática). Raciocinio y convencimiento tardaron algo más.

Estudiantes e internos, al descubrir mis expedientes clínicos anteriores escritos en inglés, gozan con "pegarme vellones". Deseo, pues, hacer públicas tanto esa conversión como mis convicciones en cuanto a este problema.

La conversión fue en Venezuela. Hará unos cinco años, intenté exponer allí, en español, un tema científico. Y me quedé mudo. No sabía suficiente español técnico para comunicarme. ¿En español, una de las lenguas principales del mundo, y la vernáculo nuestra, por añadidura! Allí decidí comenzar a escribir los expedientes en español. De ahí en adelante descubrí algunas cositas de interés.

Gallina, "hen": Lo primero fue una curiosa oposición administrativa a cambiar de idioma. A mí lo informaron una sola vez, verbalmente. Cuando lo pedí por escrito, no se me complació. Desde entonces, en múltiples ocasiones, estudiantes, internos, residentes y algunos catedráticos me han comunicado su creencia de que para conservar la "acreditación" de tal o cual hospital es necesario escribir en inglés.

Se equivocan malamente. Los americanos no son tan miopes. Lo sé por experiencia. Ahora bien, sí es necesario convencerlos de que las cosas se hacen con buenas razones.

Ante tal preocupación de mis colegas preguntamos a los representantes del Joint Commission on Accreditation of Hospitals sobre el particular. Nos informaron que ellos no objetan el español (¿cómo podrían humanamente objetar?) siempre y cuando haya un traductor en el hospital cuando a éste se le inspeccione.

Pluma, "pencil": Afianzado en mi conversión, pronto vi fundamentos muy lógicos para vencerme. Antes que nada adquirí consciencia de los muchos errores que el uso del inglés ocasiona. Eruditos, nuestros médicos desconocen que algunos miembros de nuestro personal auxiliar no

entienden sus órdenes ni sus notas clínicas. Si duro es descifrar la letra de algunos médicos, me dicen las enfermeras, cuánto más penoso resulta que nos "tiren con el difícil". Este personaje (pues lo substantivan) es por supuesto, el inglés. A mis lectores de Caguas y áreas limítrofes les será familiar ese apodito.

Así averigüé que por no preguntar el significado de "dangle the patient, b.i.d.", la enfermera sencillamente no lo cumplía, pero si escribía "sentar al borde de la cama, b.i.d.", entonces sí. Eso sirve para ilustrar mi punto, pero sobran los ejemplos. Decidí, pues, continuar escribiendo en español porque así: 1ro., evitaba errores potencialmente serios en el cuidado de mis pacientes, 2do., lograba comunicar exactamente mis deseos, 3ro., conseguía que se cumplieran mis órdenes, 4to., pulía mis conocimientos, y 5to., recuperaba de mi tartamudeo.

Lápiz, "pen": Esta disertación de año nuevo quedaría incompleta si no se aborda otro asunto.

Con merecidos bombos y platillos se reciben los cambios hechos a los programas de los cursos de medicina, pero mientras eso sucede, poca atención se da a la urgente necesidad con que se nos viene encima la educación del personal auxiliar, o como se dice ahora, de los profesionales aliados en el campo de la salud.

El espíritu de equipo, su esfuerzo colectivo, la cooperación de todos sus componentes, y otras cosas más, pesarán mucho este año y en los venideros. Responsabilidad nuestra, y muy seria, es revisar cuidadosamente la formación de este personal. ¿Es ésta uniforme? ¿intercambiable entre instituciones? ¿atiende a las necesidades del tratamiento moderno de nuestros pacientes? ¿queremos gente con destrezas prácticas o con mucho bagaje técnico?

Consideraciones como estas serán motivo de comentarios editoriales futuros. Y ojalá que los chistosos no se me adelanten con los suyos: "primero la conversión, luego la convicción, y ahora . . . las epístolas."

Jorge O. Just Viera, M. D.

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Precautions: Peripheral neuropathy may occur. A fatality has been reported. Predisposing conditions such as renal impairment, anemia, diabetes, electrolyte imbalance, vitamin B deficiency and debilitating disease may enhance such occurrence.

Adverse reactions: Nausea, emesis and diarrhea may occur; reduction in dosage may alleviate these symptoms. Sensitization appearing as cutaneous eruptions or pruritus has occurred. Hypersensitivity reactions resulting in nonfatal anaphylaxis, angioedema, pulmonary infiltration with pleural effusion and eosinophilia have been reported. Other possible

terial flora elsewhere in the body. (As with other antibacterials, superinfections may occur, but these are limited to the urinary tract. Pseudomonas is the organism most commonly implicated.)

Macrochantin works against a majority of urinary tract pathogens, including some strains of Proteus and Klebsiella-Aerobacter; however, only a small percentage of strains of Pseudomonas are susceptible.

*Due to susceptible organisms

reactions are chills, fever, jaundice, asthmatic symptoms and hypotension. Occasionally headache, dizziness, nystagmus, vertigo, drowsiness, malaise, muscular aches have occurred. Transient alopecia has been reported. Leukopenia, including granulopenia, has been reported rarely. The blood picture returned to normal following cessation of therapy with other antimicrobial agents, superinfections resistant organisms may occur. With Macrochantin however, these are limited to the genitourinary because suppression of normal bacterial flora where in the body does not occur.

Dosage: Adult: 50 to 100 mg. four times a day.

Supplied: Macrochantin (nitrofurantoin macrocrystals) Capsules of 50 mg. and 100 mg. EATON PRODUCT CODE—For easy product identification and verification—Macrochantin Capsules: mg. (F03), 100 mg. (F04).



Originators and Developers of The Nitrofurantoin
EATON LABORATORIES
Norwich International
410 Park Avenue, New York, N.Y. 1002

WHEREVER IT HURTS

HERE

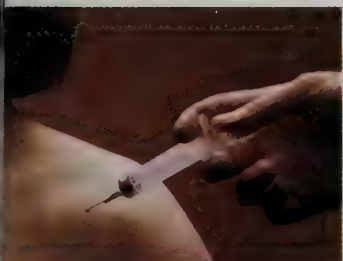
Fractures



Wherever it hurts,
Empirin Compound with
Codeine usually provides
the relief needed.

HERE

Bursitis



In general, only pain so severe
that it requires morphine is
beyond the scope of
Empirin Compound with Codeine.

prescribing convenience:
up to 5 refills in 6 months,
at your discretion (unless
restricted by state law); by
telephone order in many states.

Empirin Compound with
Codeine **No. 3**, codeine
phosphate* 32.4 mg. (gr. ½);
No. 4, codeine phosphate*
64.8 mg. (gr. 1). *Warning—
may be habit-forming. Each
tablet also contains: aspirin
gr. 3½, phenacetin gr. 2½,
caffeine gr. ½.



Burroughs Wellcome Co.
Research Triangle Park
North Carolina 27709



EMPIRIN[®] COMPOUND c CODEINE

#3, codeine phosphate* (32.4 mg.) gr. ½
#4, codeine phosphate* (64.8 mg.) gr. 1



IMPORTANT INFORMATION: This is a Schedule V substance by Federal law; diphenoxylate HCl is chemically related to meperidine. In case of overdosage or individual hypersensitivity, reactions similar to those after meperidine or morphine overdosage may occur; treatment is similar to that for meperidine or morphine intoxication (prolonged and careful monitoring). Respiratory depression may recur in spite of an initial response to Nalline® (nalorphine HCl) or may be evidenced as late as 30 hours after ingestion. LOMOTIL IS NOT AN INNOCUOUS DRUG AND DOSAGE RECOMMENDATIONS SHOULD BE STRICTLY ADHERED TO, ESPECIALLY IN CHILDREN. THIS MEDICATION SHOULD BE KEPT OUT OF REACH OF CHILDREN.

Indications: Lomotil is effective as adjunctive therapy in the management of diarrhea.

Contraindications: In children less than 2 years, due to the decreased safety margin in younger age groups, and in patients who are jaundiced or hypersensitive to diphenoxylate HCl or atropine.

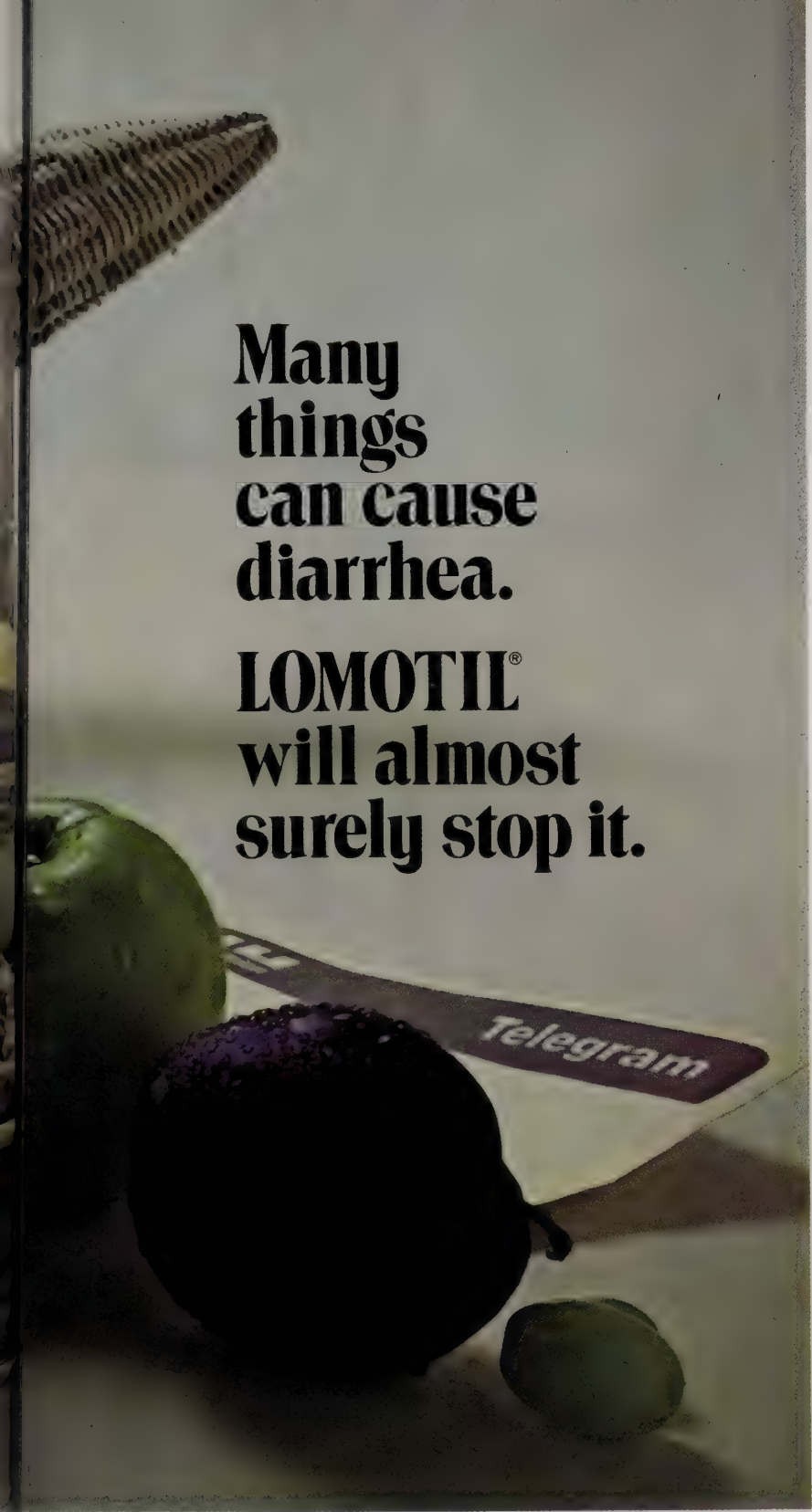
Warnings: Use with caution in young children, because of variable response, and with extreme caution in patients with cirrhosis and other advanced hepatic disease or abnormal liver function tests, because of possible hepatic coma. Diphenoxylate HCl may potentiate the action of barbiturates, tranquilizers and alcohol. In theory, the concurrent use with monoamine oxidase inhibitors could precipitate hypertensive crisis.

Usage in pregnancy: Weigh the potential benefits against possible risks before using during pregnancy, lactation or in women of childbearing age. Diphenoxylate HCl and atropine are secreted in the

breast milk of nursing mothers.

Precautions: Addiction (dependency) to diphenoxylate HCl is theoretically possible at high dosage. Do not exceed recommended dosages. Administer with caution to patients receiving addicting drugs known to be addiction prone or having a history of drug abuse. The subtherapeutic amount of atropine is added to discourage deliberate overdosage; strictly observe contraindications, warnings and precautions for atropine; use with caution in children since signs of atropinism may occur even with the recommended dosage.

Adverse reactions: Atropine effects include dryness of skin and mucous membranes, flushing and urinary retention. Other side effects with Lomotil include nausea, sedation, vomiting, swelling of the gums, abdominal discomfort, respiratory depression, numbness of the extremities, headache, dizziness, depression, malaise, drowsiness, coma, lethargy.



**Many
things
can cause
diarrhea.**

**LOMOTIL[®]
will almost
surely stop it.**

The causes of diarrhea are as varied as man's complaints and indiscretions. Because the causes of diarrhea can be obscure and because uncontrolled diarrhea can present serious problems, it is important to know a drug that will usually stop diarrhea promptly. For many physicians, the antidiarrheal drug of choice is Lomotil. It provides almost certain control of diarrhea.

It is also useful in controlling the intestinal transit time of patients with ileostomies and colostomies and the diarrhea occurring after gastric surgery.

Serious side effects are infrequent with Lomotil. It should be used with caution in young children, however, because of their variability in response. Use of Lomotil in children under two years of age is contraindicated.

**For the almost certain
control of diarrhea,**

LOMOTIL[®]
TABLETS/LIQUID

Each tablet and each 5 ml. of liquid contain:
Diphenoxylate hydrochloride 2.5 mg.
(Warning: may be habit forming)
Atropine sulfate 0.025 mg.

SEARLE

SEARLE & CO.
San Juan, Puerto Rico 00936

Address medical inquiries to:
G. D. Searle & Co., Medical Department
Box 5110, Chicago, Illinois 60680

restlessness, euphoria, pruritus, angioneurotic edema, giant urticaria and paralytic ileus.

Contraindications and administration: Lomotil is contraindicated in children less than 2 years old. Use only Lomotil liquid for children 2 to 12 years old. For children 2 to 5 years, 4 ml. (2 mg.) t.i.d.; 5 to 8 years, 4 ml. (2 mg.) q.i.d.; 8 to 12 years, 4 ml. (2 mg.) 5 times daily; adults, two tablets (5 mg.) t.i.d. to two tablets (5 mg.) q.i.d. or two regular teaspoonfuls (10 mg.) q.i.d. Maintenance dosage may be as low as one fourth of the initial dosage. Make downward dosage adjustment as soon as initial symptoms are controlled.

Overdosage: Keep the medication out of the reach of children since accidental overdosage may cause drowsiness, even fatal, respiratory depression. Signs of overdosage include flushing, lethargy or coma, hypotension, reflexes, nystagmus, pinpoint pupils, tachycardia and respiratory depression which may occur

12 to 30 hours after overdose. Evacuate stomach by lavage, establish a patent airway and, when necessary, assist respiration mechanically. Use a narcotic antagonist in severe respiratory depression. Observation should extend over at least 48 hours.

Dosage forms: Tablets, 2.5 mg. of diphenoxylate HCl with 0.025 mg. of atropine sulfate. Liquid, 2.5 mg. of diphenoxylate HCl and 0.025 mg. of atropine sulfate per 5 ml. A plastic dropper calibrated in increments of 1/2 ml. (total capacity, 2 ml.) accompanies each 2-oz. bottle of Lomotil liquid.

Dosage forms: Tablets, 2.5 mg. of diphenoxylate HCl with 0.025 mg. of atropine sulfate. Liquid, 2.5 mg. of diphenoxylate HCl and 0.025 mg. of atropine sulfate per 5 ml. A plastic dropper calibrated in increments of 1/2 ml. (total capacity, 2 ml.) accompanies each 2-oz. bottle of Lomotil liquid.



MINOCIN® made the difference in just eight days.*

Clinical Data:

Patient: 47-year-old male.

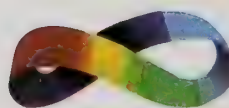
Diagnosis: Severe pyoderma, left hand.

Culture: *Staphylococcus aureus*, coagulase positive and sensitive to MINOCIN.

Temperature: 102° F

Therapy: MINOCIN Minocycline HCl Capsules, 100 mg: 200 mg *stat*, 100 mg every 12 hours. Medication began 9/7/71. By fourth day, temperature was normal and pustular lesions considerably improved. Last dose taken 9/14/71.

Concomitant therapy: None.†



Semisynthetic

MINOCIN®
MINOCYCLINE HCl

Capsules, 100 mg: 2 *stat*, 1 q 12 h.

Minocycline is a tetracycline with activity against a wide range of gram-negative and gram-positive organisms.

Contraindications: Hypersensitivity to any tetracycline.

Warnings: The use of tetracyclines during tooth development (last half of pregnancy, infancy and childhood to the age of 8 years) may cause permanent discoloration of the teeth (yellow-gray-brown). This is more common during long-term use but has been observed following repeated short-term courses. Enamel hypoplasia has also been reported. Tetracyclines, therefore, should not be used in this age group unless other drugs are not likely to be effective or are contraindicated. In renal impairment, usual doses may lead to excessive accumulation and liver toxicity. Under such conditions, use lower doses, and, in prolonged therapy, determine serum levels. Photosensitivity manifested by an exaggerated sunburn reaction has been observed in some individuals taking tetracyclines. Advise patients apt to be exposed to direct sunlight or ultraviolet light that such reaction can occur, and discontinue treatment at first evidence of skin erythema. Studies to date indicate that photosensitivity does not occur with MINOCIN Minocycline HCl. In patients with significantly impaired renal function, the antianabolic action of tetracycline may cause an increase in BUN, leading to azotemia, hyperphosphatemia, and acidosis. Pregnancy: In animal studies, tetracyclines cross the placenta, are found in fetal tissues, and can have toxic effects on the developing fetus (often related to retardation of skeletal development). Embryotoxicity has been noted in animals treated early in pregnancy. Safety of use during human pregnancy has not been established. **Newborns, infants and children:** All tetracyclines form a stable calcium complex in any bone-forming tissue. Prematures, given oral doses of 25 mg/kg. every 6 hours, demonstrated a decrease in fibula growth rate, reversible when drug was discontinued. Tetracyclines are present in the milk of lactating women who are taking a drug of this class. Safe

use has not been established in children under 13.

Precautions: Use may result in overgrowth of nonsusceptible organisms, including fungi. If superinfection occurs, institute appropriate therapy. In venereal diseases when coexistent syphilis is suspected, darkfield examination should be done before treatment is started and blood serology repeated monthly for at least four months. Patients on anticoagulant therapy may require downward adjustment of such dosage. Test for organ system dysfunction (e.g., renal, hepatic and hemopoietic) in long-term use. Treat all Group A beta hemolytic streptococcal infections for at least 10 days. Avoid giving tetracycline in conjunction with penicillin.

Adverse Reactions: (Common to all tetracyclines, including MINOCIN) GI: (with both oral and parenteral use): anorexia, nausea, light-headedness, vomiting, diarrhea, glossitis, dysphagia, enterocolitis, inflammatory lesions (with monilial overgrowth) in anogenital region. **Skin:** maculopapular and erythematous rashes. Exfoliative dermatitis (uncommon). Photosensitivity is discussed above ("Warnings"). **Renal toxicity:** rise in BUN, dose-related (see "Warnings"). **Hypersensitivity reactions:** urticaria, angioneurotic edema, anaphylaxis, anaphylactoid purpura, pericarditis, exacerbation of systemic lupus erythematosus. When given in high doses, tetracyclines may produce brown-black microscopic discoloration of thyroid glands; no abnormalities of thyroid function studies are known to occur. In young infants, bulging fontanels have been reported following full therapeutic dosage, disappearing rapidly when drug was discontinued. **Blood:** hemolytic anemia, thrombocytopenia, neutropenia, eosinophilia.

NOTE: Concomitant therapy: Antacids containing aluminum, calcium, or magnesium impair absorption; do not give to patients taking oral minocycline. Studies to date indicate that MINOCIN is not notably influenced by foods and dairy products.

*Indicated in infections due to susceptible organisms. Culture and sensitivity testing recommended. Tetracyclines are not the drugs of choice in the treatment of any staphylococcal infection.

†Case Report, Clinical Investigation Department, Lederle Laboratories.



LEDERLE LABORATORIES, A Division of American Cyanamid Company, Pearl River, New York 10965

436-2

NOTICIAS

XII CONGRESO MEDICO SOCIAL PANAMERICANO Y XI ASAMBLEA DE LA CONFEDERACION MEDICA PANAMERICANA - 18 al 23 de marzo de 1973 - Quito, Ecuador. Para información favor de escribir a: XII Congreso Médico Social Panamericano, Casilla 2269, Quito - Ecuador. Dirección Telefónica: Fedemédicos Quito.

The Florida Chapter of the American College of Emergency Physicians and the Emergency Department Nurses Association will present a Postgraduate Seminar on Emergency Medicine at the Playboy Plaza Hotel, Miami Beach, Florida from March 21-24, 1973 — Co-sponsor: University of Miami School of Medicine. This four-day program is designed to present current pertinent and practical information for those most intimately involved in delivering emergency medical care — the emergency physician, general and family physician, emergency nurse, hospital administrator, emergency medical technician, and community health planner. The latest knowledge and technology in emergency medicine will be surveyed by the guest faculty. Each registrant will receive a complimentary copy of the seminar's proceedings.

For information contact: J. Clifford Findeiss, MD, Florida Chapter, American College of Emergency Physicians, Postgraduate Seminar on Emergency Medicine, 11130 S. W. 173rd Terrace, Miami, Florida 33157.

From the Washington Office, American Medical Association:

THE MONTH IN WASHINGTON

Congressional leaders have given national health insurance a high priority, but the new Congress convening this month may not act on it until late this year or even next year.

Senate Democratic Leader Mike Mansfield of Montana assigned the legislation "the highest priority" and expressed confidence that a national health insurance program will be approved during the next two years by the 93rd Congress.

The key congressman on this legislation, Rep. Wilbur D. Mills (D., Ark.), chairman of the House Ways and Means Committee, has described the 93rd Congress as moving "to fashion a national health insurance program which the great bulk of Americans can support."

Another piece of legislation of major importance to the medical profession that will be before the 93rd Congress deals with health maintenance organizations (HMOs). The Senate last year approved a bill authorizing a broad HMO program and the House Health Subcommittee approved a much more limited program.

Democrats remain in control of Congress and the key

congressmen on health care legislation will continue to be Mills; Kennedy, chairman of the Senate Health Subcommittee; Rep. Paul G. Rogers (D.-Fla.), chairman of the House Health Subcommittee; and Sen. Russell B. Long (D.-La.).

The Bureau of Narcotics and Dangerous Drugs has proposed restricting sales of nine barbiturates which were described as highly addictive and linked to 1,771 suicides and deaths in 17 months.

The General Accounting Office, Congress' watchdog on federal spending, issued a voluminous report on the nation's health care system with recommendations that it estimated could save several billions of dollars annually.

The basic recommendations were for better construction, design and planning, better usage of health care facilities, and more emphasis on preventive medicine and group practice.

The year-long GAO study was commissioned by Congress originally to survey the Hill-Burton hospital construction program. The Senate Labor and Public Welfare Committee later asked the GAO to expand it to include all aspects of health care.

One out of four patients was reported to receive more hospital care than necessary. The report said that reducing hospital stays an average of one day would in effect add 96,000 beds to the nation's hospitals. It was estimated that putting patients needing long-time care, as opposed to acute, in special facilities would not only be less expensive but would make available 126,000 beds in general hospitals. Expansion of home health care programs would reduce the need for 20,000 hospital beds the report said. Sharing of services by regional groups of hospitals could increase efficiency. For example, the 90,000 hospital beds allotted to obstetrics could be reduced by 38,000.

CIGARETTE SMOKING AND LUNG CANCER

CHICAGO — Further evidence that cigarette smoking increases the incidence of lung cancer is reported in the November issue of the Journal of the American Medical Association.

The Philadelphia Pulmonary Neoplasm Research Project followed the medical histories of a group of 6,027 volunteers for a period of ten years. During that time, 121 of those studied developed lung cancer. All were smokers. Using the daily cigarette consumption of these patients as a standard, the authors formulated risk ratios for different types of lung tumors.

Bronchial cancer was found to be twice as likely if the patient smoked over 20 cigarettes a day. Poorly differentiated squamous-cell tumors were apparently unrelated to the degree of cigarette smoking, but greatly differentiated squamous-cell tumors were twice as common in patients who smoked 20 or more cigarettes a day.

Instrucciones para los Autores

El Boletín acepta para su publicación artículos relativos a medicina y cirugía y las ciencias afines. Igualmente acepta artículos especiales y correspondencia que pudiera ser de interés general para la profesión médica.

El artículo, si se aceptara, será con la condición de que se publicará únicamente en esta revista.

Para facilitar la labor de revisión de la Junta Editora y la del impresor, se requiere de los autores que sigan las siguientes instrucciones:

Manuscrito: El manuscrito completo, incluyendo las leyendas y referencias deberán estar escritos a maquina a doble espacio y por un solo lado de cada página, en duplicado y con amplio margen. En página separada deberá incluirse lo siguiente: título, nombre del autor (es) y su grado (ej: MD, FACP), ciudad donde se hizo el trabajo, el hospital o institución académica, patrocinadores del estudio, y si un artículo ha sido leído en alguna reunión o congreso, así debe hacerse constar como una nota al calce.

El manuscrito debe comenzar con una breve introducción en la cual se especifique el propósito del mismo. Las secciones principales (como por ejemplo: materiales y métodos) deben identificarse como un encabezamiento al centro y en letras mayúsculas.

Artículos referentes a resultados de estudios clínicos o investigaciones de laboratorio deben organizarse bajo los siguientes encabezamientos: Introducción, Materiales y Métodos, Resultados, Discusión, Resumen (en español e inglés), Reconocimiento y Referencias.

Artículos referentes a estudios de casos aislados deben organizarse en la siguiente forma: Introducción, Materiales y Métodos si es aplicable, Observaciones del Caso, Discusión, Resumen (en español e inglés), Reconocimientos y Referencias.

Nomenclatura: Deben usarse los nombres genéricos de los medicamentos. Podrán usarse también los nombres comerciales, entre paréntesis, si así se desea. Se usará con preferencia el sistema métrico de pesos y medidas.

Tablas: Las tablas deben aparecer en hojas separadas. Estas deben incluir el título y el número de la tabla (romano). Los símbolos de unidades deben limitarse al encabezamiento de las columnas. Se deben omitir líneas verticales y horizontales en la tabla.

Figuras: Las fotografías y microfotografías se someterán como copias en papel de lustre, sin montar. En el reverso de la figura debe aparecer el número de la figura (arábigo) y el autor y debe indicarse la parte superior.

Referencias: Las referencias deben ser numeradas sucesivamente de acuerdo con su aparición en el texto. Los números deben aparecer en paréntesis al nivel de la línea u oración. Al final de cada artículo las referencias deben aparecer en el orden numérico en que se citan en el texto. Estas deben seguir el estilo o patrón del "Index Medicus", el cual se describe a continuación:

Para artículos de Revista

Apellido (s), e iniciales del nombre del autor (es), nombre de la revista, volumen, primera página y año.

Koppisch E: Bol Asoc Med P Rico 46: 505, 1954.

Para citación de Libros

Apellido (s), e iniciales del autor (es), título, edición, casa editora, ciudad, año y página.

Wintrobe MM: Clinical Hematology, 3rd Ed Lea and Febiger, Philadelphia 1952 p 67.

Más de tres autores añadir: et al.

Deben usarse solamente las abreviaturas indicadas en el "Cumulative Index Medicus" que publica la Asociación Médica Americana.

Como guía de referencia para preparar su artículo puede usar la publicación Advice to Authors que publica la Scientific Publications Division, American Medical Association, 535 N Dearborn Street, Chicago, Illinois, 60610.

Instructions to Authors

The Boletín will accept for publication contributions relating to the various areas of medicine, surgery and allied medical sciences. Special articles and correspondence on subjects of general interest to physicians will also be accepted. All material is accepted with the understanding that it is to be published solely in this journal.

In order to facilitate review of the article by the Editorial Board and the work of the printer, the authors must conform with the following instructions:

Manuscripts: The entire manuscript, including legends and references should be typewritten double spaced in duplicate with ample margins. A separate title page should include the following: title, authors and their degrees (e. g. MD, FACP), city where the work was done, hospital or academic institutions,

acknowledgment of financial sponsors, and if the paper has been presented at a meeting the place and date should be given.

The manuscript should start with a brief introductory paragraph or paragraphs which should state its purpose. The main sections (for example, Materials and Methods) should be identified by center headings in capital letters.

Articles reporting the results of clinical studies or laboratory investigation should be organized under the following headings: Introduction, Material and Methods, Results if indicated, Discussion, Summary in English and Spanish, Acknowledgments if any, and References.

Nomenclature: Generic names of drugs should be used; trade names may also be given in parenthesis, if desired. Metric units of measurements should be used preferentially.

Tables: These should be typed on separate sheets with the title and table number (Roman) centered. Symbol for units should be confined to the column headings. Vertical and horizontal lines should be omitted.

Figures: Photographs and photomicrographs should be submitted as glossy prints, unmounted. They should be labeled in the back with the name of the authors and figure number (Arabic) and the top should be indicated. Legends to the figures should

be typed on a separate sheet.

References: These should be numbered serially as they appear in the text. The number should be enclosed in parenthesis on the line of writing and not as superscript numbers. At the end of the article references should be listed in the numerical order in which they are first cited in the text. This list should conform to the Style of the Index Medicus and should be punctuated as in the following examples.

For journal articles: Surname and initials of author (s), name of journal, volume, first page and year.

Koppisch E: Bol Asoc Med P Rico 46: 505, 1954.

For Books: Surname and initials of author (s), title, edition, publishing house, City, year and page.

Wintrobe MM: Clinical Hematology, 3rd Ed Lea and Febiger, Philadelphia 1952 p 67.

More than three authors add: et al.

Abbreviations will conform to those used in the Cumulative Index Medicus, published by the American Medical Association.

For aid in preparing your manuscript refer to the publication Advice to Authors available from the Scientific Publications Division, American Medical Association, 535 N Dearborn St., Chicago, Illinois 60610.

ANUNCIO

Una gran oportunidad de hacerse de un magnífico apartamento. El mismo consta de 5 oficinas y 2 baños. 3,000 pies cúbicos. Cerca del ascensor y frente a las escaleras. Tiene estacionamiento privado. Está en sitio céntrico de área comercial. En el primer piso del edificio está un Centro de Rayos X. Apartamento 3A, Edificio Norte, Condominio Las Torres, Bayamón. Para información: Sra. Marrero, Calle 6 P3 Ext. La Milagrosa, Bayamón, P. R. - Después de las 3:00 p.m.

FUTUROS TRABAJOS A PUBLICARSE

1. "Doctors, Defenses and the Age of Informed Consent" — Lou Ashe, JD, LL.M.
2. "Urinary Calculi in Puerto Rico" — Julio V. Rivera, MD, FACP.
3. "Development, Classification, Visual Prognosis and Treatment of Diabetic Retinopathy — José A. Berrocal, MD
4. "Las Enfermedades Respiratorias en Puerto Rico - Problema Actual" — Waldemar E. Santiago, MD. - Editor
5. "La Gastritis Micropoliposa - Potencialidad Neoplásica" — A. Rodríguez Olleros, MD, et al.
6. "Grave Problema de la Retinopatía Diabética" - Editorial - José A. Berrocal, MD.

INDICE DE ANUNCIANTES

1. *Burroughs Wellcome Co.*
2. *Eaton Laboratories*
3. *Geigy Pharmaceuticals*
4. *Lederle Laboratories*
5. *Roche Laboratories*
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Vitamina E	30 Unidades Internacionales
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Potasio (como sulfato)	5 mg.

Posología: Adultos y niños mayores de 6 años - 1 tableta diaria.

Presentación: Frascos de 30 y 90

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Effect on mental acuity: Usually minimal on proper maintenance dosage.

Safety: An excellent clinical record. In general use, the most common side effects reported have been drowsiness, ataxia and confusion, particularly in the elderly and debilitated.

**in relief of clinically
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Indications: Relief of anxiety and tension occurring alone or accompanying various disease states.

Contraindications: Patients with known hypersensitivity to the drug.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation, or in women of childbearing age requires that its potential benefits be weighed against its possible hazards.

Precautions: In the elderly and debili-

tated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the

elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

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BOLETIN

ASOCIACION MEDICA
DE PUERTO RICO

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SHELVES



Vol. 65

Febrero 1973

No.2



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and the psychotropic action of Valium® (diazepam).

Before deciding to make Valium (diazepam) part of your treatment plan, check on whether or not the patient is presently taking drugs and, if so, what his response has been. Along with the medical and social history, this information can help you determine initial dosage, the possibility of side effects and the ultimate prospects of success or failure.

While Valium can be a most helpful adjunct to your counseling, it should be prescribed only as long as excessive psychic tension persists and should be discontinued when you decide it has accomplished its therapeutic task. In general, when dosage guidelines are followed, Valium is well tolerated (see Dosage). For convenience it is available in 2-mg, 5-mg and 10-mg tablets.

Drowsiness, fatigue and ataxia have been the most commonly reported side effects.

Until response is determined, patients receiving Valium should be cautioned against engaging in hazardous occupations requiring complete mental alertness, such as driving or operating machinery.



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Nutley, N.J. 07110

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

Dosage: Individualize for maximum beneficial effect.

Adults: Tension, anxiety and psychoneurotic states, 2 to 10 mg b.i.d. to q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed; adjunctively in skeletal muscle spasm, 2 to 10 mg t.i.d. or q.i.d.; adjunctively in convulsive disorders, 2 to 10 mg b.i.d. to q.i.d. **Geriatric or debilitated patients:** 2 to 2½ mg, 1 or 2 times daily initially, increasing as needed and tolerated. (See Precautions.) **Children:** 1 to 2½ mg t.i.d. or q.i.d. initially, increasing as needed and tolerated (not for use under 6 months).

Supplied: Valium® (diazepam) Tablets, 2 mg, 5 mg and 10 mg; bottles of 100 and 500. All strengths also available in Tel-E-Dose® packages of 1000.

Valium® (diazepam)

To help you manage excessive psychic tension

BOLETIN

ASOCIACION MEDICA DE PUERTO RICO



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insulin secretion from the pancreas. And this may be important to the dieting diabetic.

In adult-onset, nonketotic diabetics uncontrolled by diet alone...

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Tablets of 25 mg.

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Capsules of 50 and 100 mg.

Indications: Stable adult diabetes mellitus; sulfonylurea failures, primary and secondary; adjunct to insulin therapy of unstable diabetes mellitus.

Contraindications: Diabetes mellitus that can be regulated by diet alone; juvenile diabetes mellitus that is uncomplicated and well regulated on insulin; acute complications of diabetes mellitus (metabolic acidosis, coma, infection, gangrene); during or immediately after surgery where insulin is indispensable; severe hepatic disease; renal disease with uremia; cardiovascular collapse (shock); after disease states associated with hypoxemia.

Warnings: Use during pregnancy is to be avoided.

Precautions: 1. *Starvation Ketosis:* This must be differentiated from "insulin lack" ketosis and is characterized by ketonuria which, in spite of relatively normal blood and urine sugar, may result from excessive phenformin therapy, excessive insulin reduction, or insufficient carbohydrate intake. Adjust insulin dosage, lower phenformin dosage, or supply carbohydrates to alleviate this state. **Do not give insulin without first checking blood and urine sugar.** 2. *Lactic Acidosis:* This drug is not recommended in the presence of azotemia or in any clinical situation that predisposes to sustained hypotension that could lead to lactic acidosis. To differentiate lactic acidosis from ketoacidosis, periodic

determinations of ketones in the blood and urine should be made in diabetics previously stabilized on phenformin, or phenformin and insulin, who have become unstable. If electrolyte imbalance is suspected, periodic determinations should also be made of electrolytes, pH, and the lactate-pyruvate ratio. The drug should be withdrawn and insulin, when required, and other corrective measures instituted immediately upon the appearance of any metabolic acidosis.

3. *Hypoglycemia:* Although hypoglycemic reactions are rare when phenformin is used alone, every precaution should be observed during the dosage adjustment period particularly when insulin or a sulfonylurea has been given in combination with phenformin. **Adverse Reactions:** Principally

gastrointestinal; unpleasant metallic taste, continuing to anorexia, nausea and, less frequently, vomiting and diarrhea. Reduce dosage at first sign of these symptoms. In case of vomiting, the drug should be immediately withdrawn. Although rare, urticaria has been reported, as have gastrointestinal symptoms such as anorexia, nausea and vomiting following excessive alcohol intake. (B) 98-146-103-D (6/72)

For complete details, including dosage, please see full prescribing information.

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Because the taste is good.

- ☐ promptly relieves hyperacidity
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aluminum and magnesium hydroxides with simethicone



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We're not against all her E. coli...

only the E. coli in her
urinary tract



Macrochantin (nitrofurantoin macrocrystals) is exceptionally effective against E. coli. But it confines its antibacterial action to the urinary tract. It is indicated for the treatment of cystitis,* pyelitis* and pyelonephritis*...nothing else.

Macrochantin is not indicated for therapy of any systemic infection. *And it does not suppress normal bac-*

**Basic in cystitis,* pyelitis,*
pyelonephritis***

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Macrochantin® Capsules
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Indications: Macrochantin (nitrofurantoin macrocrystals) is indicated for the treatment of pyelonephritis, pyelitis and cystitis due to E. coli, enterococci, Staph. aureus or a small percentage of strains of Pseudomonas, when demonstrated to be susceptible by in vitro susceptibility testing. Also for treatment of such infections when due to some susceptible strains of Klebsiella-Aerobacter and Proteus. It is not indicated for treatment of associated renal cortical or perinephric abscesses, systemic infections or prostatitis, or in any genitourinary tract infections other than pyelonephritis, pyelitis and cystitis.

Contraindications: Anuria, oliguria or extensive impairment of renal function is a contraindication. The drug is contraindicated for infants under one month and in pregnant patients at term. The drug should not be administered to persons who have shown hypersensitivity to nitrofurantoin.

Warnings: Macrochantin may cause hemolytic anemia of the primaquine sensitivity type, apparently linked to a glucose-6-phosphate dehydrogenase deficiency. This deficiency is found in 10 per cent of Negroes and in a small percentage of ethnic groups of Mediterra-

nean and Near-Eastern origin. Such patients should be observed closely while receiving nitrofurantoin. Discontinue the drug at any sign of hemolysis. Hemolysis ceases on withdrawal. Superinfections may occur, most commonly due to Pseudomonas.

Usage in pregnancy: THE SAFETY OF NITROFURANTOIN DURING PREGNANCY AND LACTATION HAS NOT BEEN ESTABLISHED. IT SHOULD NOT BE USED IN WOMEN OF CHILDBEARING POTENTIAL UNLESS THE EXPECTED BENEFITS OUTWEIGH THE POSSIBLE HAZARDS.

Precautions: Peripheral neuropathy may occur. A fatality has been reported. Predisposing conditions such as renal impairment, anemia, diabetes, electrolyte imbalance, vitamin B deficiency and debilitating disease may enhance such occurrence.

Adverse reactions: Nausea, emesis and diarrhea may occur; reduction in dosage may alleviate these symptoms. Sensitization appearing as cutaneous eruptions or pruritus has occurred. Hypersensitivity reactions resulting in nonfatal anaphylaxis, angioedema, pulmonary infiltration with pleural effusion and eosinophilia have been reported. Other possible

terial flora elsewhere in the body. (As with other antibacterials, superinfections may occur, but these are limited to the urinary tract. Pseudomonas is the organism most commonly implicated.)

Macrochantin works against a majority of urinary tract pathogens, including some strains of Proteus and Klebsiella-Aerobacter; however, only a small percentage of strains of Pseudomonas are susceptible.

*Due to susceptible organisms.

reactions are chills, fever, jaundice, asthmatic symptoms and hypotension. Occasionally headache, dizziness, nystagmus, vertigo, drowsiness, malaise and muscular aches have occurred. Transient alopecia has been reported. Leukopenia, including granulocytopenia, has been reported rarely. The blood picture has returned to normal following cessation of therapy. As with other antimicrobial agents, superinfections by resistant organisms may occur. With Macrochantin, however, these are limited to the genitourinary tract because suppression of normal bacterial flora elsewhere in the body does not occur.

Dosage: Adult: 50 to 100 mg. four times a day

Supplied: Macrochantin (nitrofurantoin macrocrystals) Capsules of 50 mg. and 100 mg
EATON PRODUCT CODE—For easy product identification and verification—Macrochantin Capsules 50 mg. (F03), 100 mg. (F04)



Originators and Developers of The Nitrofurans
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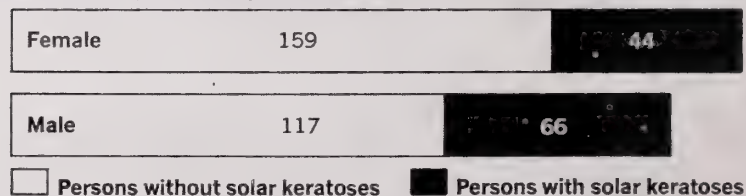
What it means to live and work in Tipton County, Tennessee

**Persons who are white and
over 40 have one chance in four
of having solar keratoses...
which may be premalignant**

An epidemiologic study* conducted in Tipton County, Tennessee, revealed that 28.5% of white persons over 40 had solar keratoses; most had multiple lesions. Cluster sampling projected an estimated prevalence of 32.5% for white males and 19.5% for white females.

Though this is an unusually high percentage of affected persons, these lesions can occur in any white population, wherever people work or play out of doors.

**Prevalence of solar keratoses in white persons
over 40 in Tipton County, Tennessee**



*Data on file, Hoffmann-La Roche Inc., Nutley, New Jersey.



Solar, actinic, senile keratoses

Called by many names, the typical lesion is flat or slightly elevated, brownish or reddish in color, papular, dry, adherent, rough, sharply defined; usually multiple lesions, chiefly on exposed portions of the skin.

Sequence/selectivity of response

Erythema in areas of lesions may begin after several days of therapy; height of reaction usually in affected areas* usually occurs within 70 weeks, declining after discontinuation of therapy. Since this response is so predictable, lesions that do not respond should be biopsied to rule out the presence of a frank neoplasm.

Cosmetic results

Cosmetic results are highly favorable. Incidence of scarring is low—important with multiple facial lesions. Efudex should be applied with care near the eyes, nose and mouth.

5% cream—a Roche exclusive

Only Roche formulates the 5% cream... high in patient acceptability... high in clinical efficacy, especially for lesions of hands and forearms... economical.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Multiple actinic or solar keratoses.

Contraindications: Patients with known hypersensitivity to any of its components.

Warnings: If occlusive dressing used, may increase inflammatory reactions in adjacent normal skin. Avoid prolonged exposure to ultraviolet rays. Safe use in pregnancy not established.

Precautions: If applied with fingers, wash hands immediately. Apply with care near eyes, nose and mouth. Lesions failing to respond or recurring should be biopsied.

Adverse Reactions: Local—pain, pruritus, hyperpigmentation and burning at application site most frequent; also dermatitis, scarring, soreness and tenderness. Also reported—insomnia, stomatitis, suppuration, scaling, swelling, irritability, medicinal taste, photosensitivity, lacrimation, leukocytosis, thrombocytopenia, toxic granulation and eosinophilia.

Dosage and Administration: Apply sufficient quantity to cover lesion twice daily with nonmetal applicator or suitable glove. Usual duration of therapy is 2 to 4 weeks.

How Supplied: Solution, 10-ml drop dispensers—containing 2% or 5% fluorouracil on a weight/weight basis, compounded with propylene glycol, tris(hydroxymethyl)amino-methane, hydroxypropyl cellulose, parabens (methyl and propyl) and disodium edetate.

Cream, 25-Gm tubes—containing 5% fluorouracil in a vanishing cream base consisting of white petrolatum, stearyl alcohol, propylene glycol, polysorbate 60 and parabens (methyl and propyl).

an alternative to conventional therapy **Efudex**[®] (fluorouracil) cream/solution



Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, N.J. 07110



With the means at hand to drastically reduce the number of deaths each year from uterine cancer, we have embarked on a nationwide, life-saving program. Its goal is a Pap test by 1976 for every woman 20 years or older to whom the test is applicable, and for younger women at risk. An ambitious program, doctor, and one which can only be realized with your help.

We are faced with these facts: only 53% of women over

20 have ever had a Pap test; only 20% get a Pap test periodically; each year about 43,000 new cases are diagnosed; this year 12,000 women in this country will die of uterine cancer. And about 75% of these deaths will result from cervical cancer — as you know, almost 100% curable when diagnosed early and treated promptly.

We hope to reach women in the target group not only with the message about the *vital*

Pap test, but also with the urgency of including it in the *regular* health checkup. The mortality rate from uterine cancer could thus be dramatically curtailed.

Clearly action is called for. Coordinated action — involving the doctor, the patient, the American Cancer Society — a partnership for life.

a partnership for life



American Cancer Society



Dx: Hiatal Hernia

Rx: Maalox[®]

Maalox[®] relieves the symptoms of hiatal hernia by neutralizing gastric hyperacidity. It doesn't constipate. And its taste is pleasant, nonfatiguing—all important considerations in the treatment of a long-term condition like hiatal hernia.

In short, Maalox is the kind of antacid that makes symptomatic relief of hiatal hernia as decisive as its diagnosis.

Maalox[®] Suspension

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(5 fl. oz. [plastic bottle] and 12 fl. oz.).

Maalox[®] No. 1 Tablets (0.4 Gm.)

—no sugar and low in sodium.

Maalox[®] No. 2 Tablets (0.8 Gm.)

—the "chew" tablet with double antacid action.

Maalox[®]

(Magnesia and Alumina Oral Suspension, Rorer)


the number one antacid



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Integument!

Our skin—the human integument—covers us, defines us, protects us. But skin is subject to cuts, burns, abrasions. And infections. Neosporin Ointment fights infection by providing broad antibacterial action against susceptible skin invaders. It contains antibiotics that are rarely used systemically, reducing the risk of sensitization.



INDICATIONS: *Therapeutically*, used as an adjunct to appropriate systemic therapy for topical infections, primary or secondary, due to susceptible organisms, as in: • infected burns, skin grafts, surgical incisions, otitis externa • primary pyodermas (impetigo, ecthyma, sycosis vulgaris, paronychia) • secondarily infected dermatoses (eczema, herpes, and seborrheic dermatitis) • traumatic lesions, inflamed or suppurating as a result of bacterial infection.

Prophylactically, the ointment may be used to prevent bacterial contamination in burns, skin grafts, incisions, and other clean lesions. For abrasions, minor cuts and wounds accidentally incurred, its use may prevent the development of infection and permit wound healing.

CONTRAINDICATIONS: Not for use in the external ear canal if the eardrum is perforated. This product is contraindicated in those individuals who have shown hypersensitivity to any of the components.

PRECAUTION: As with other antibiotic preparations, prolonged use may result in overgrowth of nonsusceptible organisms and/or fungi. Appropriate measures should be taken if this occurs. Articles in the current medical literature indicate an increase in the prevalence of persons allergic to neomycin. The possibility of such a reaction should be borne in mind.

Complete literature available on request from Professional Services Dept. PML.

NEOSPORIN[®] Ointment

(POLYMYXIN B-BACITRACIN-NEOMYCIN)

Each gram contains: Aerosporin[®] brand Polymyxin B Sulfate 5,000 units; zinc bacitracin 400 units; neomycin sulfate 5 mg. (equivalent to 3.5 mg. neomycin base); special white petrolatum q.s. In tubes of 1 oz. and ½ oz. and ¼ oz. (approx.) foil packets.



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Research Triangle Park
North Carolina 27709

DOCTORS, DEFENSES AND THE AGE OF INFORMED CONSENT

Lou Ashe, JD, LLM

Nearly three decades ago, in a case wherein it was contended specialists in X-Ray had injured the patient by an overdose in the treatment of a pilonidal cyst, a learned federal judge observing both sides of the coin made these observations:

"Malpractice is hard to prove. The physician has all the advantages of position. He is presumably an expert. The patient is a layman. The physician knows what is done and what is its significance. The patient may or may not know what is done. . . He judges chiefly by results. The physician has the patient in his confidence, disarmed against suspicion. Physicians, like lawyers, are loathe to testify a fellow craftsman has been negligent, especially when he is highly reputable in professional character. . . in short, the physician has the advantage of knowledge and of proof. . ."

"On the other hand malpractice is a serious charge. The physician is not an insurer of health. He undertakes only for the standard of skill possessed generally by others practicing in his field, and for care which they would give in similar circumstances. He must have latitude for play of reasonable judgment, and this includes room for not too obvious or gross errors according to the prevailing practice of his craft. Generally the standard must be shown by experts and so use the departure from it. But there are cases in which the result of medical or surgical treatment considered in light of the circumstances attending and following it may warrant an inference of negligence."

Delivered to the Puerto Rico Medical Association, Friday, November 18, 1972. Mr. Ashe is a senior partner in the firm of Belli, Ashe, Ellison and Choulos of San Francisco and Los Angeles, California. He has served as past national president of the American Trial Lawyers' Association. Noted as a writer and lecturer, he serves presently as Dean of the International Academy of Trial Lawyers. Mr. Ashe is actively engaged in medico-legal litigation at the trial level and has contributed generously to the literature of both specialists. He holds both an Honorary Doctor of Humanities and a Doctor of Laws degree in recognition of his work.

Please write Mr. Ashe for complete bibliography.

Here we are, two ancient and honorable professions, living our professional lives within circumscribed and demanding rules of ethics and statutory regulations, both bound to grave responsibilities to the public and to the courts.

As I conceive it, we have not gathered to discuss RIGHT V. WRONG, but RIGHT V. RIGHT and with such a concept, we are mutually involved with an honest consideration of the tedium, intellectual and physical toil, the time, money, anxieties and often the degradations and assaults to the psyche inherent in the preparing and investiture of a man as a physician. And, having attained this valued status, both the legal and medical professions are one in their belief that the right of the physician to practice his profession into the specialties and sub-specialties free of unwarranted governmental interference or over-bearing judicial frustration should be assured.

But — there is another right in this special regard. . . the right of every individual to be free of pain, suffering, mutilation and other forms of pathological insult and even death which may be imposed upon him through the negligence, ignorance, or, if you will, cavalier professional disdain and at times the abandonment of those who occupy a fiduciary status in their relationships with him and in whom he has properly placed his trust.

A. *Historically Speaking. . .*

Viewed historically, the professional liability of the medical practitioner is almost as old as the personal injury action. Probably the first recorded case in Anglo-American law goes back to the year 1374 when one J. Mort, allegedly undertook to treat a wounded hand. He was stated to have "acted in such a negligent manner as to maim the hand." The court, while dismissing the action for technical reasons, nevertheless indicated that if the surgeon had done as well as he was able and had employed all his diligence in administering to the patient "it is not right that he should be held culpable", thus reflecting the standard of care suggested by the Hippocratic Oath.

In 1767 an English court held a surgeon liable for ignorance and lack of skill. In *Seare v. Prentice* (1807),

the court relied heavily upon the statements of the great law writer, Blackstone, as to the implied contract of "everyone who undertakes any offers, employment, trusts or duty. . . to perform it with integrity, diligence and skill. And if by his want of either of these qualities, any injury accrues to individuals, they have therefore their remedy in damages.

Probably the earliest of the reported *American* cases on professional liability of doctors may be found in *Cross v. Guthery*, in which the court held a complaint sufficient which alleged that the defendant, having held himself out as a practicing physician, skilled in surgery, had undertaken to perform a mastectomy on the plaintiff's wife "with skill and safety" and that defendant "performed such operation in the most unskillful, ignorant and cruel manner, contrary to all well-known rules and principles of practice in such cases." (1794).

The Pennsylvania Court later stated that the obligation of a physician was "to treat the case with diligence and skill. . . such reasonable skill and diligence as are ordinarily exercises in his profession . . . such as thoroughly educated surgeons ordinarily employ." (1853).

In *Leighton v. Sargent*, (1853), the pronouncement of the Court is almost modern in its basic concepts of what is malpractice. Here the court said in part that the undertaking of a physician or surgeon was:

" 1. That he possesses that reasonable degree of learning, skill and experience which is ordinarily possessed by the professors of the same art or science, and which is ordinarily regarded by the community, by those conversant with that employment, as necessary and sufficient to qualify him to engage in such business. . . 2. That he will use reasonable and ordinary care and diligence in the exertion of his skill and the application of his knowledge, to accomplish the purpose for which he is employed. He does not undertake for extraordinary care or extraordinary diligence, anymore than he does for uncommon skill . . . 3. In stipulating to exert his skill, and apply his diligence and care, the medical or other professional men contract to use their best judgment. . . "

Thus, it is clear that guidelines have been set over a century ago and succinctly stated — A physician is liable to his patient for failure to exercise requisite skill and care. To put it another way, the physician or doctor assumes toward the patient the obligation to exercise such reasonable care and skill in that behalf as is usually exercised by physicians or surgeons of good standing, of the same system or school or practice in the medical community in which he resides, or in similar communi-

ties under similar circumstances having due regard to the condition of medical and surgical science at the time.

The evolving law of malpractice reflects now the concern of our top-level Appellate Courts to protect the patient who has not been informed fully regarding the nature and hazards of the treatment proposed to be undertaken. The Courts will not permit the patient to be abandoned in any way and the doctrine of *res ipsa loquitur* (to be discussed elsewhere) has now come into its full expression to aid the plaintiff in certain specific instances in establishing a *prima facie* case against the professional who is treating him. A physician occupies a position of trust in relation to his patient and is required to deal honestly with him with regard to all aspects of treatment, diagnosis and prognosis.

B. *The Plaintiff's Case Doesn't Get Off the Ground Unless. . .*

1. He can prove that the physician or hospital he seeks to charge as responsible for his injuries was negligent. It should be noted that for the most part the rules which a physician follows in his professional life are of his own creation. They are internal and fixed within the profession itself. These standards are established, with few exceptions, by one or more local doctors summoned as expert witnesses and testifying in a particular case. Actually, the law does exhibit quite a tender regard for the insulation of defendant physicians by these standards. The problems have arisen and the hostility has been increased when the courts have permitted external standards to come into play, fixed by the community at large under doctrines of reasonableness. It is under this concept that the doctrine of *res ipsa loquitur* has arisen, which in some cases makes it possible to prove a case without special testimony of medical experts and by resorting to the common sense and knowledge of the jurors themselves.

2. Even proof of negligence or carelessness in any particular case is not enough. It is necessary for the plaintiff to prove that the negligence or carelessness complained of was the proximate cause, the competent producing cause, of his injuries, or, as the case may be, of his death. Most usually, this element of the case is a question of fact for the jury. However, in an ordinary case, it requires expert medical testimony not only to establish the fact of deviation from the standards of care, but the element of proximate cause as well. The cases are legion in which the defendants have attempted to explain the injuries sustained by the patient upon a variety of causative medical factors, for none of which they would be liable.

3. Even where the plaintiff succeeds and arrives at a jury verdict, there still sits the judge as the thirteenth juror, who may do any of the following:

- a. Reduce the amount of the judgment as excessive;
- b. Grant a new trial;
- c. Reverse the judgment, notwithstanding the verdict; or,
- d. At the close of plaintiff's case declare a non-suit, and if not then, at the close of the entire case direct a verdict for defendant.

C. *Here Come De Judge, But He Loses*

It may give you some consolation to know that on the whole, juries are quite objective in these matters.

Recently, a Maine jury returned a verdict in favor of the defendant in a malpractice suit brought by the Presiding Judge of the county. Another judge was imported to try the case in the judge's own courtroom. Here are the brief facts:

"On November 30, 1967, the judge had consulted the physician for treatment of an oral lesion. The physician again saw the judge on two occasions in December. It was not until March 18, 1968, that a biopsy was performed. The diagnosis was then made of epidermoid carcinoma.

The judge filed a medical malpractice lawsuit against the physician. The judge charged the physician with "gross negligence" for failing to order a biopsy in November. The judge requested damages totalling \$350,000. Portions of the judge's teeth, taste buds and palate had been removed in preventive surgery.

At trial, an expert medical witness testified that cancer cells must double 25 times before they are palpable. Two other expert medical witnesses testified that this doubling takes from eight to 700 days. The physician being sued argued that, theoretically, a biopsy may not have been indicated for another two years.

The jury deliberated less than four hours before returning a verdict in favor of the physician."

Hospital Records: Their Format, Content and Medico-Legal Significance

A. *Patient's Right to Access*

In California, the patient's right to copies of medical records is for practical purposes unrestricted by virtue of legislation adopted in 1968.

Thus, Section 1158, actual part of the Uniform Evidence Code of 1967, permits any lawyer who pre-

sents written authorization to require the production by any physician, surgeon, dentist, registered nurse, dispensing optician, registered physical therapist, and a variety of other medical personnel, including licensed clinical laboratory bioanalysis and technologists, or from any licensed hospital, all of a patient's records and his or its custody or contents. These records must be made available for inspection and copying by the attorney or his representative within 5 days.

As a practical matter, medical communities and hospitals have generally become aware of this procedure, and are usually cooperative, permitting copying services to photocopy records in their custody or control for transmission to attorneys so authorized. Hospital records, depending upon the meticulousness with which they have been developed, and the manner in which they truly reflect the details of the treatment and all medical procedures involved, often can spell the difference between success and failure in the defense of a doctor when he is charged with deviation from standards of care.

Experience has shown repeatedly that the absence of crucial data, the failure of a physician to give specific orders, or the failure of a nurse to record significant signs or symptoms and the occasional obvious attempt to doctor not only the patient, but the record itself, can prove disastrous to a defendant physician's position in the courtroom.

Recently we resolved a tragic case involving the death of an Air Force Lt. Colonel brought to a small municipal hospital in critical condition, bleeding intra-abdominally, with signs and symptoms of severe shock and hemorrhage which should have been recognized by any prudent physician and surgeon, and which the Supervisor of Nurses in fact recognized, as was reflected in the chart post mortem. The treating physician well knew and admitted the "rules of the game" and precisely what was required of him under reasonable standards of good medical practice. The problems arose from his failure to implement his mental processes. We quote in part:

Q. It is one of the duties of a treating physician and surgeon, Doctor, to use his Order Sheet to give specific instructions for the care of any patient and certainly, sir, one who is critically ill, is it not, Doctor?

A. It is the duty to give instructions that you feel necessary for that patient and his benefit.

Q. And it is the duty of the doctor to write out on the Order Sheet all orders for medication which the physician believes are reasonably

calculated to help their recovery.

A. That is usual.

Q. And to give appropriate orders for the continued care of the patient?

A. Yes, that is usual, too.

With the patient still in shock, his abdominal hemorrhaging undiagnosed, with no orders written for the continued close observation of his failing vital signs, a nurse's aid was assigned to the 11:00 pm shift. For reasons she could not explain, and with no order, she gave this patient a shot of morphine. She was unaware of any order to check his vital signs and report all deteriorations. In the face of a failing blood pressure, and exhibiting the signs of severe shock, without orders, this nurse did not call the doctor until after she found the patient dead at 1:00 a.m.

B. The Importance of a Hospital Record or Medical Report in an Injury Case.

Where the patient is conscious and oriented and capable of offering the details of his history, it is of extreme importance as to who takes the initial history and the manner in which it is recorded. In every case that reaches the trial stage, the hospital record is bound to be one of the important exhibits. Occasionally, in so-called "teaching hospitals", a number of interns may take the initial history, and depending upon their patience; training and, above all, their ability to *listen*, may depend much of the injured patient's care.

When the patient is incapable of communication, if any history at all is recorded its source should be clearly indicated. Indifference in developing the case history and particularly the past history of an injured person, his or her sensitivities, allergies, prior surgery, prior cardiac or pulmonary involvements, among other things, are all of the essence. I would also add that when the patient has at any time been anaesthetized, that good standards would demand that the records reflect any reaction to a particular anaesthetic agent. For example, if a patient has once had a reaction to halothane (fluothane), he should not again be exposed to this agent.

Very few physicians under cross-examination would be willing to suggest that they had failed in any way to record everything the patient had told them. Too often, some matter remains undisclosed on records of past history which lives to haunt the plaintiff in his lawsuit. For example, the plaintiff's treating physician, under cross-examination, may be asked:

Q. Doctor, I assume that you were interested in the past history of the patient, in any accidents he may have been involved in which he may

have in any way caused injury to his upper or lower spine.

A. Yes, normally I would want to know that.

Q. Would this be a significant entry to make on the history, Doctor?

A. Yes, it would.

Q. Did Mr. Jones tell you that just 11 months prior to the time he claims cervical and lumbar injury in this case, he was injured in a rear-end accident, hospitalized for 2 weeks, wore a cervical collar for 3 weeks and went through some 18 traction treatments?

A. I don't recall.

Q. Well, if he had, observing good practice, you would have recorded it, wouldn't you?

A. Yes, I would.

This plaintiff may now be quite well discredited in the eyes of the jury.

If the patient has, in fact, withheld information, then he must bear this cross. But if he attempted to advise the physician of this fact and was ignored, his dilemma must be obvious.

Hospital Liability

A. The Implications of Darling vs. Charleston Community Hospital

Dorrence Darling, II, a minor, 18 years old, broke his leg in a college football game. He was taken to the emergency room of the defendant hospital. One Dr. Alexander was on call. Assisted by hospital personnel, he applied traction and casted the leg. Very shortly Dorrance was in great pain, and his toes protruding from the cast became swollen and dark in color. Eventually they became cold and insensitive. On the evening of November 6, the doctor "notched" the cast around the toes. The next afternoon he cut the cast about three inches up from the foot. November 8, using a Stryker saw, he split the sides of the cast. However, in the course of cutting he cut the minor's leg on both sides. The nurses observed blood and seepage from the cast. There was a stench in the room described by one witness as revolting. On November 19 the youngster was removed to the Barnes Hospital in St. Louis under the care of the head of orthopedic surgery, who found the leg contained considerable amounts of dead tissue caused, in his opinion, by the interference with the blood circulation caused by the swelling or hemorrhaging in the leg against the constriction of the cast. Several operations followed in a futile attempt to save the leg. Suit was brought against Dr. Alexander and the hospital.

The doctor settled. Trial followed against the hospital only.

The case has been the subject of many medical as well as legal publications, seminars and conferences. Basically, the acute question presented was: In a situation where the hospital has not actually deviated from prevailing standards of care but was negligent in failing to adhere to its own rules and regulations which required that it provide competent physicians for the care of its patients, can it be held liable if such negligence results in injury to a patient? The Supreme Court of Illinois answered in the affirmative and sustained the damages awarded plaintiff.

The evidence for the plaintiff demonstrated that the hospital administrator did not exercise reasonable care to ensure that the hospital's doctors were qualified. No request had been made of the medical staff nor the governing board to determine the competency of the physician involved. This violated the hospital's own rules. However, let me emphasize that the creation of the rules does not in and of itself set an absolute standard. The rules remain as evidence which may be considered by the jury who must determine the reasonableness of the requirements all to the end that they may assess whether reasonable care has been exercised by the hospital in the light of the apparent risks to be encountered.

Hospitals accredited by the Joint Commission of Accreditation of Hospitals and who are governed by the public licensing authorities must exert strong effort to assure the observance of those standards set by both the private and public authorities by its lay as well as its professional staffs and personnel. Viewed realistically, juries are sensitive to injuries resulting from the hospital's violations of its own rules and regulations. In a case I was privileged to try some years ago, the patient suffered a series of "nightmarish" surgical procedures which were generated by the failure to remove an 11x14 laparotomy sponge following a cholecystectomy. The introduction of the hospital's regulations with regard to the proper procedures for sponge and needle counts, admonitions of the hazards of carelessness in this regard and the "anaesthesia chart" which indicated — "Sponge count - O. K." were all very persuasive, among other indicting evidence, in the jury's very substantial verdict against the hospital.

The way to avoid malpractice suits in this and other areas is to remove the causes which courts seize upon to assess liability. Courts have cautioned that:

"A hospital may be liable in tort for permitting its facilities to be used by an unlicensed person or

where a licensed person has committed malpractice with the knowledge of the hospital or under circumstances putting it on notice of such wrongful act."

To re-emphasize:

"The lay administration of the hospital cannot ignore or close its eyes to what is going on professionally within the walls of the institution."

In the light of *DARLING* and some of its progeny, I am impelled to caution you further that the long entertained concept that a hospital does not undertake to act through its doctors and nurses, but undertakes simply to procure them to act on their own responsibility no longer reflects the fact in this modern day world.

"Present day hospitals . . . do far more than furnish facilities for treatment. They regularly employ on a salary basis a large staff of physicians, nurses and interns, as well as administrative and manual workers . . . they charge patients for medical care and treatment . . . Certainly, the persons who avail themselves of 'hospital facilities' expect that the hospital will attempt to cure him, not that its nurses or other employees will act on their own responsibility."

In the very dramatic California case of *Quintal v. Laurel Grove Hospital, et al.*, a normal, six year-old boy entered the hospital for correction of an inward deviation of his eyes, suffered a cardiac arrest during anesthesia and severe brain damage resulting in his becoming a spastic quadriplegic, blind and mute. Action was brought against the anaesthetist, the ophthalmological surgeon and the hospital. For the moment, let's examine *only* the reasoning of the court in affirming the involvement of the hospital itself. On the morning of the surgery, the boy patient was apprehensive, agitated and had a rising temperature. There was impressive testimony that in this non-emergency situation surgery and anaesthesia should have been delayed. When the "arrest" occurred, the operating surgeon, unqualified to open the chest, left the O. R. and dashed into the hall looking for help, which he found, but too late. The court, first making it clear that the negligence of the anaesthesiologist and the surgeon did not in and of itself impose liability on the hospital unless there were some form of agency existing, stated:

"There was evidence from which an agency should be inferred. Dr. T.—— testified that he had an active part in the management of the hospital, was its acting administrator, and a member of the board of directors. As administrator, he worked out

an agreement with a group of anesthesiologists with whom he was connected to supply a proper anesthesiologist upon demand of the hospital . . . Under this agreement (as required) the group sent . . . the available doctor on the list."

The hospital furnished the nurses and operating room, and all the equipment used by the anesthesiologist. The boy's mother, as required by the hospital officials, signed a "Consent to Operate" which authorized the surgeon "to administer such treatment and to have administered such anesthetics as found necessary. The form, provided by the hospital, was witnessed by two hospital employees. Upon this evidence the court concluded that a jury question existed and that is, the jury could have, with legal justification, found the hospital liable.

These are but a few examples of the type of negligence which has come to be known as "corporate liability". A Connecticut court has defined corporate negligence as the "failure of those entrusted with the task of providing accommodations and facilities necessary to carry out the charitable purpose of the corporation to follow in a given situation the established standard of conduct to which the corporation should conform. Professor Arthur F. Soutwick, of Michigan University long recognized as an authority on hospital liability offers this prognosis:

"Hospitals are, and for the foreseeable future will continue to be the primary vehicle for the control and enhancement of standards of quality of care. . . Court decisions in liability cases will recognize the changing and central role of the hospital and gradually expand concepts of corporate negligence."

Recognizing the *DARLING* case as a prime example, the good Professor yet cautions that the "case warrants careful analysis" so as to avoid confusion and misunderstanding as to the role of the hospital administration in the total picture of providing quality medical care to the American public.

B. *Hospital Liability: Some Examples*

1. *The Case of the Misused Cross Matched Blood:*

Mrs. Buck was a 39-year old expectant mother. A Caesarean delivery and possible hysterectomy being anticipated, cross matched blood was prepared and set aside for a possible transfusion and held in the blood bank. After Caesarean delivery and hysterectomy, the following regrettable events were permitted to occur. She was not admitted to the recovery room. Vital signs were taken sloppily and then only for six hours. After six hours, no vital signs were taken. Although the signs were not in themselves alarming, the trend was. The pulse rate went up and the blood pressure went down. Three hours later, Mrs. Buck had a convulsion. Without consent of the surgeon, the blood being held for her was given to another patient in violation of hospital policy. No effort was made to replenish it. When the patient's blood loss was finally recognized, it was too late for additional blood to be cross matched. Result? The patient bled to death. The jury awarded the survivors \$225,000.00. (April, 1972).

(To be continued)

URINARY CALCULI IN PUERTO RICO: II. SEASONAL INCIDENCE

Julio V. Rivera, MD, FACP

In a previous report on the crystalline composition of urinary stones we pointed out the lack of basic epidemiological data about this common condition in Puerto Rico (1). These data may supply leads which could guide therapeutic or preventive efforts.

The present study was directed to the collection of information on the prevalence of stone disease in a hospital population in Puerto Rico and to exploration of possible effects of climatic factors on this rate.

Materials and Methods

The records of the hospital's Admission Room for the years 1965, 1966 and 1967 were reviewed and a count was made of the number of patients examined in whom a diagnosis of urinary calculus had been made. Patients were counted whether they were admitted to the hospital or not. The total number of patients (all causes) examined at the Admission Room during the same period was also determined in order to establish any possible seasonal variation in overall activity of the service. Their number were tabulated for each month.

Because of the fact that only a small proportion of patients who come to the hospital's Admission Room because of urinary calculi are finally admitted to the hospital, the data included in this study relate more to out-patients than to in-patients. The diagnosis in these patients was based on the occurrence of ureteral colic, the examination of the urine and roentgenograms of the abdomen. Intravenous pyelograms were made when the diagnosis was not clear or when symptoms persisted suggesting impaction of the calculus or the presence of infection. Patients were instructed to strain their urine and to bring the stone for examination when passed.

In order to study the possible relationship between climatic conditions and the incidence of urinary calculi, we obtained from the U. S. Weather Bureau Office in San Juan data (2) as to temperature, precipitation, relative humidity, wind velocity and sky cover for the same three years. The data used refers to determinations at the San Juan International Airport which we have assumed reflect the conditions to which the majority of our patients were exposed to. A high proportion of them reside in the San Juan metropolitan area and nearby towns.

From the Medical Service, Veterans Administration Hospital, San Juan, Puerto Rico; and the Department of Medicine, University of Puerto Rico School of Medicine.

Results

Incidence of Urinary Calculi

During the three-year period covered by the study 910 patients came to the Admission Room because of symptoms related to urinary calculi. This represents approximately 3 percent of all patient visits.

When the number of visits of patients with urinary calculi is tabulated for each month, a recurrent pattern is evident each year (Table I, fig. 1). During the months of November or December to April or May the number of visits is lower than it is from June to October, with a peak in July 1966 and October 1965 and 1967. That this cycle is not related to an increase in the number of patients seen at the Admission Room is apparent when the number of these is reviewed for each year or when the ratio of patients with calculi to the total is calculated.

A chi-square test applied to the monthly percentages of calculi to all diagnoses comparing the months of January through June to July through December showed the difference in rates to be significant at the 0.005 level ($\chi^2 = 24.95$).

Climatological Data

During the three years of the study (Tables II and

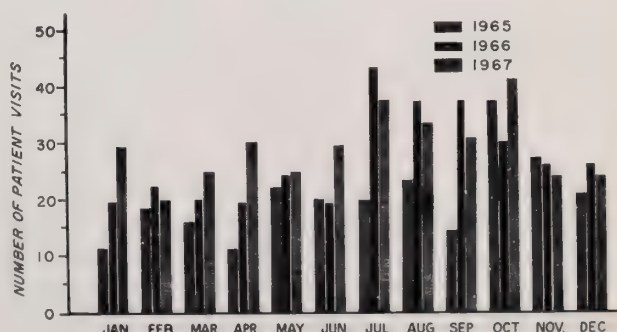


Fig. 1: Number of patient visits (to Admission Room of Veterans Administration Hospital, San Juan, Puerto Rico, 1965 - 1967) for symptoms related to urinary calculi.

TABLE I: MONTHLY NUMBER OF PATIENTS WITH CALCULI
AND TOTAL NUMBER EXAMINED AT ADMISSION ROOM

Month	1965			1966			1967			1965-1967				1965-1967	
	Calculi	All *	Percent	Calculi	All	Percent	Calculi	All	Percent	Calculi No.	Percent	All No.	Percent	Calculi (Percent)	All
Jan.	11	685	1.61	19	826	2.30	29	900	3.22	59	6.48	2411	7.99	2.44	
Feb.	18	707	2.55	22	738	2.98	20	860	2.33	60	6.59	2305	7.64	2.60	
Mar.	16	747	2.14	20	842	2.37	25	944	2.64	61	6.70	2533	8.39	2.40	
Apr.	11	685	1.61	19	932	2.03	30	873	3.43	60	6.59	2490	8.25	2.40	
May	22	652	3.37	24	937	2.56	25	1026	2.43	71	7.80	2615	8.66	2.71	
Jun.	20	739	2.70	19	1044	1.81	29	894	3.24	68	7.47	2677	8.87	2.54	
Jul.	20	783	2.55	43	880	4.88	37	919	4.02	100	10.99	2582	8.55	3.87	
Aug.	23	748	3.07	37	917	4.03	33	1006	3.28	93	10.22	2671	8.85	3.48	
Sep.	14	674	2.08	37	850	4.35	31	894	3.46	82	9.01	2418	8.01	3.39	
Oct.	37	790	4.68	30	748	4.01	41	945	4.33	108	11.87	2519	8.35	4.28	
Nov.	27	732	3.69	26	805	3.22	24	947	2.53	77	8.46	2484	8.23	3.09	
Dec.	21	727	2.89	26	852	3.05	24	898	2.67	71	7.80	2477	8.21	2.86	
TOTALS	240	8669	2.77	322	10371	3.10	348	11106	3.13	910	100	30182	100	3.01	

* All refers to number of patients with all diagnoses examined during the same period.

TABLE II: NUMBER OF CALCULI AND TEMPERATURE FOR 1965, 1966 AND 1967

Month	1965			1966			1967		
	No.	Ave.Temp.(°F)	Temp. > 90° (°F)	No.	Ave. Temp.	Temp. > 90°	No.	Ave.Temp.	Temp. > 90°
Jan.	11	74.7	0	19	77.4	0	29	76.6	0
Feb.	18	75.9	0	22	76.7	0	20	76.3	0
Mar.	16	77.7	0	20	78.1	3	25	75.9	0
Apr.	11	77.7	0	19	78.5	4	30	78.0	0
May	22	78.9	0	24	79.5	0	25	79.7	0
Jun.	20	80.3	0	19	81.0	2	29	81.8	7
Jul.	20	81.7	3	43	82.1	3	37	82.1	1
Aug.	23	81.5	0	37	82.6	4	33	82.2	3
Sep.	14	82.2	7	37	81.1	0	31	81.8	5
Oct.	37	81.5	3	30	80.0	1	41	81.4	4
Nov.	27	79.8	0	26	77.5	0	24	80.4	2
Dec.	21	77.4	1	26	77.1	0	24	77.5	0

III), the lowest monthly average temperature was recorded in January for 1965 (74.7° F), in December for 1966 (77.1° F) and in March for 1967 (75.9° F). The highest average monthly temperature recorded was 82.2° F during the month of September in 1965, 82.6° F in August in 1966 and 82.2° F in August in 1967. Thus the difference between the average temperature between the warmest and the coolest months was 7.5° F in 1965, 5.5° F in 1966 and 6.3° F in 1967.

Temperatures 90° F and above were only recorded during the months of June to November, most often in September and October in 1965 and 1967. In 1966 this pattern changed somewhat with temperatures 90° F and above occurring as early as March and only once from September on.

Although during the months of January to April skies tended to be clear as measured by "percentage of possible sunshine" and "mean sky cover sunrise to sunset" there are considerable month to month varia-

TABLE III: CALCULI AND SELECTED CLIMATOLOGICAL DATA

Month	No. Calculi*	Ratio Calculi/All +	Ave.Temp. +	No. Days + > 90°	Relative Humidity 2 PM (Percent) +	Ave.Wind Velocity ‡	Percent Poss. Sunshine +	Precipitation (inches) +
Jan.	59	2.4	76.3	0	64	8.8	65	2.34
Feb.	60	2.6	76.3	0	64	10.5	62	1.78
Mar.	61	2.4	77.2	3	61	10.2	79	2.32
Apr.	60	2.4	78.0	4	61	11.3	74	2.89
May	71	2.7	79.3	0	71	11.2	62	8.28
Jun.	68	2.5	81.0	9	69	9.8	62	5.86
Jul.	100	3.9	82.0	7	70	11.3	67	4.96
Aug.	93	3.5	82.1	7	67	10.2	73	5.43
Sep.	82	3.4	81.7	12	69	8.2	66	5.71
Oct.	108	4.3	81.0	8	69	6.7	64	6.18
Nov.	77	3.1	79.2	2	68	7.9	61	5.64
Dec.	71	2.9	77.3	1	67	9.8	57	4.80

* Total for 3 years.

+ For 3 years.

‡ 1966 and 1967 only. Data not available for 1965.

tions and the pattern varied a lot from year to year.

Average wind velocity was slowest for each year during September, October and November even though this is the "hurricane season".

Average relative humidity in 1965 and 1966 was lowest during the months of February to April and highest from August to October in 1965 and 1966. The records for 1967 show no clear seasonal pattern. Rainfall was highest in May (8.28 inches), lowest from January to April (1.78 - 2.89 inches).

The time relationship between the incidence of calculi and some of the climatological data is shown in Table III. It is apparent that symptoms due to calculi occur most often during the months of July to October which are the warmest ones and during which humidity is highest, skies tend to be more overcast, rain is plentiful and wind velocity is relatively low.

Discussion

The results of this study indicate a recurrent yearly pattern in the incidence of symptoms attributable to urinary calculi. A seasonal variation similar to that found by us has been reported from northern Florida by Leonard (3). A relation of climatic factors to the incidence of urinary calculi is supported by several other studies which relate a high rate to a warm climate (4, 5, 6). In the present study a higher environmental temperature, increased relative humidity, increased precipitation and slower winds prevailed during the months when the peak incidence of symptomatic disease was seen.

The remarkable finding shown here is that the relatively small changes in weather conditions observed should appear to be related to the production of disease. Perhaps the brief but more marked temperature peaks which occurred most often during certain months of the year may be more important than the monthly average ambient temperatures. This may be suggested by the findings of the peak incidence of symptoms due to calculi during the month of July in 1966 as opposed to October in 1965 and 1967. In 1966, but not in 1965 or 1967, temperatures above 90° F were recorded as early as March. The importance of brief changes in the physicochemical conditions of the urine at the renal papillae as the initial event in calculus formation has been emphasized by Vermeulen (7). Ambient factors, through their effect on body temperature may lead to increased loss of water through the skin and respiratory tract. Transitory reduction in urinary volume and increased concentration of urinary crystalloids is the probable direct precipitating factor in the formation of the initial nidus. Other possible mechanisms such as variations in urinary calcium concentration, or in the levels of antiricketic factors (8) which may also be connected to climatic conditions may deserve study.

The fact that the yearly peak in the incidence of symptoms appears later than the peak of the average temperature curve may be interpreted as being related to the time required for the growth of the original microscopic crystalline nidus to the size required to produce obstruction and thus become clinically evident (8).

The possible clinical implications of our finding of an apparent "calculus season" in Puerto Rico are obvious. Preventive measures directed at the reduction of increased crystalloid concentration in the urine should be reinforced during the time of augmented risk.

Summary

A three-year study at a general hospital in Puerto Rico of patients seeking emergency treatment for renal colic reveals a yearly recurrent cycle of increased occurrence during the months of July to October. This coincided or immediately followed that period of the climatic cycle when higher temperatures, increased relative humidity, increased precipitation and slower winds prevail. It is suggested that these factors, through the production of increased urinary crystalloid concentrations or other mechanisms, may trigger the formation of calculi.

Possible therapeutic implications of this seasonal variation in the management of stone disease in Puerto Rico are suggested.

Resumen

Un estudio durante tres años consecutivos del número de enfermos atendidos en la sala de admisiones de un hospital general en Puerto Rico por síntomas relativos a cólico renal reveló un ciclo anual en el cual su número era significativamente menor durante los meses de julio a octubre. Durante estos mismos meses coincide un aumento en la temperatura ambiental, la humedad relativa, la lluvia y una velocidad promedio de los vientos relativamente baja.

Se sugiere que factores ambientales pueden, mediante la producción de un aumento en la concentración urinaria de cristaloides u otro mecanismo patofisiológico, precipitar la formación de cálculos urinarios. Estas observaciones pudieran tener implicaciones terapéuticas en el manejo de esta frecuente condición.

Acknowledgment

The climatological data was kindly supplied by Mr. Robert J. Calvesbert of the U. S. Department of Commerce, Isla Verde Airport, San Juan, Puerto Rico. Mrs. Irma Valdés assembled the data on patients examined at the Admission Room. The statistical analysis was carried out by Mr. Emanuel Lerner at the Eastern Research Support Center, Veterans Administration Hospital, West Haven, Connecticut. Their valuable assistance is appreciated.

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Adverse Reactions: Drowsiness, excessive dryness of nose, throat or mouth; nervousness; or insomnia. Also, nausea, vomiting, epigastric distress, diarrhea, rash, dizziness, weakness, chest tightness, angina pain, abdominal pain, irritability, palpitation, headache, incoordination, tremor, dysuria, difficulty in urination, thrombocytopenia, leukopenia, convulsions, hypertension, hypotension, anorexia, constipation, visual disturbances, iodine toxicity (acne, parotitis).

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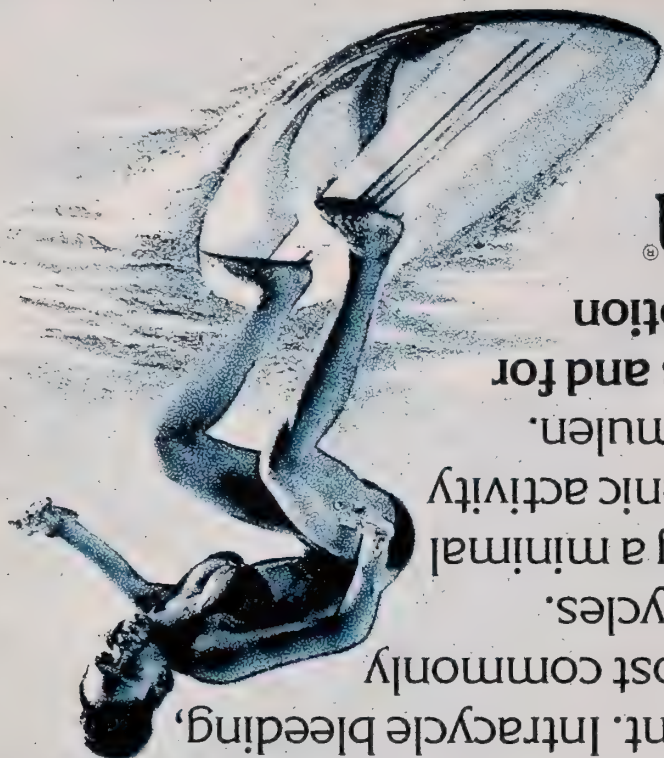
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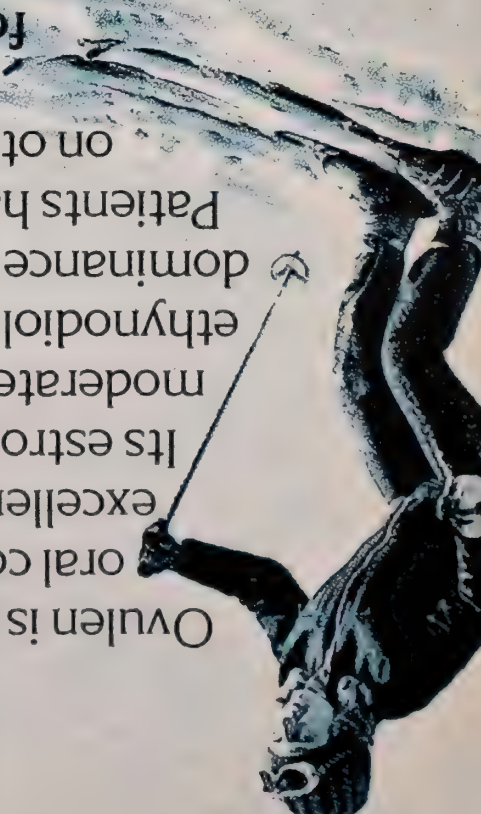
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Demulen®

Each white tablet contains
ethynodiol diacetate 1 mg/ethinyl estradiol 50 mcg

Actions—Ovulen and Demulen act to prevent ovulation by inhibiting the output of gonadotropins from the pituitary gland. Ovulen and Demulen depress the follicle-stimulating hormone (FSH) and the luteinizing hormone (LH).

Special note—Oral contraceptives have been marketed in the United States since 1960. Reported pregnancy rates vary from product to product. The effectiveness of the sequential products appears to be somewhat lower than that of the combination products. Both types provide almost completely effective contraception.

An increased risk of thromboembolic disease associated with the use of hormonal contraceptives has now been shown in studies conducted in both Great Britain and the United States. Other risks, such as those of elevated blood pressure, liver disease and reduced tolerance to carbohydrates, have not been quantitated with precision.

Long-term administration of both natural and synthetic estrogens in sub-primate animal species in multiples of the human doses increases the frequency of some animal carcinomas. These data cannot be transposed directly to man.

The possible carcinogenicity due to the estrogens can be neither affirmed nor refuted at this time. Close clinical surveillance of all women taking oral contraceptives must be continued.

Indication—Ovulen and Demulen are indicated for oral contraception.

Contraindications—Patients with thrombophlebitis, thromboembolic disorders, cerebral apoplexy or a past history of these conditions, markedly impaired liver function, known or suspected carcinoma of the breast, known or suspected estrogen-dependent neoplasia and undiagnosed abnormal genital bleeding.

Warnings—The physician should be alert to the earliest manifestations of thrombotic disorders (thrombophlebitis, cerebrovascular disorders, pulmonary embolism and retinal thrombosis). Should any of these occur or be suspected the drug should be discontinued immediately.

Retrospective studies of morbidity and mortality conducted in Great Britain and studies of morbidity in the United States have shown a statistically significant association between thrombophlebitis, pulmonary embolism, and cerebral thrombosis and embolism and the use of oral contraceptives. There have been three principal studies in Britain¹ leading to this conclusion, and one² in this country. The estimate of the relative risk of thromboembolism in the study by Vessely and Doll² was about sevenfold, while Sartwell¹ and associates³ in the United States found a relative risk of 4.4, meaning that the users are several times as likely to undergo thromboembolic disease without evident cause as nonusers.¹ The American study also indicated that the risk did not persist after discontinuation of administration and that it was not enhanced by long-continued administration. The American study was not designed to evaluate a difference between products. However, the study suggested that there might be an increased risk of thromboembolic disease in users of sequential products. This risk cannot be quantitated, and further studies to confirm this finding are desirable.

Discontinue medication pending examination if there is sudden partial or complete loss of vision, or if there is a sudden onset of proptosis, diplopia or migraine. If examination reveals papilledema or retinal vascular lesions medication should be withdrawn.

Since the safety of Ovulen and Demulen in pregnancy has not been demonstrated, it is recommended that for any patient who has missed two consecutive periods pregnancy should be ruled out before continuing the contraceptive regimen. If the patient has not adhered to the prescribed schedule the possibility of pregnancy should be considered at the time of the first missed period. A small fraction of the hormonal agents in oral contraceptives has been identified in the milk of mothers receiving these drugs. The long-range effect to the nursing infant cannot be determined at this time.

Precautions—The pretreatment and periodic physical examinations should include special reference to the breasts and pelvic organs, including a Papaniocolau smear since estrogens have been known to produce tumors, some of them malignant, in five species of subprimate animals. Endocrine and ovarian function tests may be affected by treatment with Ovulen or Demulen. Therefore, if such tests are abnormal in a patient taking Ovulen or Demulen, it is recommended that they be repeated after the drug has been withdrawn for two months. Under the influence of progestogen-estrogen preparations possibly liver function tests may increase in size. Because these agents may cause some degree of fluid retention, conditions which might be influenced by this factor, such as epilepsy, migraine, asthma, cardiac or renal dysfunction, bleeding per vaginam, nonfunctional causes should be borne in mind. In undiagnosed bleeding per vaginam adequate diagnostic measures are indicated.

Patients with a history of psychic depression should be carefully observed and diagnosed bleeding per vaginam adequate diagnostic measures are indicated.

The drug discontinued if the depression recurs to a serious degree. Any possible influence of prolonged Ovulen or Demulen therapy on pituitary, ovarian, adrenal, hepatic or uterine function awaits further study. A decrease in glucose tolerance has been observed in a significant percentage of patients on oral contraceptives. The mechanism of this decrease is obscure. For this reason, diabetic patients should be carefully observed while receiving Ovulen or Demulen therapy.

The age of the patient constitutes no absolute limiting factor, although treatment with Ovulen or Demulen may mask the onset of the climacteric. The pathologist should be advised of Ovulen or Demulen therapy when relevant specimens are submitted. Susceptible women may experience an increase in blood pressure following administration of contraceptive steroids.

Adverse reactions observed in patients receiving oral contraceptives—A statistically significant association has been demonstrated between uses of oral contraceptives and the following serious adverse reactions: thrombophlebitis, pulmonary embolism and cerebral thrombosis.

Although available evidence is suggestive of an association, such a relationship has been neither confirmed nor refuted for the following serious adverse reactions: neuro-ocular lesions, e.g., retinal thrombosis and optic neuritis.

The following adverse reactions are known to occur in patients receiving oral contraceptives: nausea, vomiting, gastrointestinal symptoms (such as abdominal cramps and bloating), breakthrough bleeding, spotting, change in menstrual flow, amenorrhea during and after treatment, edema, chloasma or melasma, changes in appetite, cystitis-like syndrome, headache, nervousness, dizziness, changes in weight, hirsutism, loss of scalp hair, erythema multiforme, erythema nodosum, hemorrhagic eruption and itching.

The following laboratory results may be altered by the use of oral contraceptives: hepatic function; increased sulfobromophthalen retention and other thyroid function; increase in PBI and butanol extractable protein bound iodine; tests: coagulation tests; increase in prothrombin, Factors VII, VIII, IX and X, and decrease in T₃ uptake values; methyrapone test and pregnanediol determination.

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Indication—Enovid-E is indicated for oral contraception.

The Special Note Contraindications, Warnings, Precautions and Adverse Reactions listed above for Ovulen and Demulen are applicable to Enovid-E and brand of norethynodrel with mestranol.

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Where "The Pill" Began

DEVELOPMENT, CLASSIFICATION, VISUAL PROGNOSIS AND TREATMENT OF DIABETIC RETINOPATHY

José A. Berrocal, MD

If at the age of 20 diabetes is diagnosed, the risk of blindness at the age of 30 is only 0.1 percent, and it increases to 3.5 percent at the age of 50 (a 35 fold increase). By comparison, for the general population, the risk of blindness from all causes at age 30 is 0.09 percent and at age 50 is only 0.15 percent (a 1.6 fold increase). At the age of 50, therefore, the diabetic is about 23 times more likely to be blind than the non-diabetic patient (2). The numerical magnitude of diabetic blindness is underscored by the observation that as many as 11-12 percent of the blind population in the United States owes its visual deficits to diabetes. In other countries, such as Denmark, the percentage has been as high as 23 percent (3). Visual disability in diabetes can be caused by retinopathy, cataract, rubeosis iridis (with secondary glaucoma), refractive change, or by a combination of these diseases. Of these, diabetic retinopathy and secondary glaucoma are the major causes of blindness.

A study prepared in September 1971 by the Harvard School of Public Health estimates that compared to the current 154,700 persons blind from diabetic retinopathy, by the year 2,000, a staggering 573,500 will be blind, more than the number blind from all causes today.

The disease is predicted to overtake cataract and glaucoma and become the leading cause of blindness in the coming decade.

Development of diabetic retinopathy

Most cases of diabetes are inherited, i. e., they are in a sense, primary. One of the most common late sequelae is diabetic retinopathy, a term encompassing all pathologic phenomena in the retina. Diabetic retinopathy has also been observed in patients with a variety of other diseases which, in turn, lead to carbohydrate intolerance as a secondary manifestation. These include the following: Cushing's syndrome, pan-

createctomy, acromegaly, hemochromatosis, chronic pancreatitis, and Werner's syndrome.

The preponderance of evidence suggests, therefore, that a chemical aberration in carbohydrate metabolism is the common etiologic forerunner of diabetic retinopathy. Regardless of basic etiology, approximately 2 percent of all diabetics become blind from retinopathy alone. This prevalence is approximately 10 times greater than that of blindness from all causes in the general population.

What factors are related to the development of diabetic retinopathy? Duration of diabetes appears to be the primary factor affecting the frequency of retinopathy. If diabetes is diagnosed below the age of 30, for example, and lasts for 5-9 years, approximately 10 percent or less of the affected individuals will demonstrate retinopathy. When the diabetes is diagnosed below the age of 30 and lasts for 15 years, however, approximately 50 percent of the individuals will have observable retinopathy. When the diabetes is diagnosed below the age of 30 and then lasts for more than 25 years, 80-90 percent of the individuals are found to have retinopathy (3).

In addition to duration of the systemic disease, "Metabolic control" may affect certain forms of retinopathy. Caird and Knowles have summarized evidence that the frequency of retinopathy may be reduced and the age of onset raised if regulation of diabetes is particularly strict during the first five years following discovery of the systemic disease. (4, 5). However, once most retinal lesions are established, metabolic control has little, if any, influence on the retinopathy.

Classification of Diabetic Retinopathy

Zwenk's classification of diabetic retinopathy is a very simple and practical way of attempting uniformity throughout the world (12).

The (a) non-proliferative stage refers to the absence of neovascularization. This stage does not threaten blindness. However (b) macular edema often occurs

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resulting in loss of central vision.

The non-proliferative stage occurs more often in the senile onset diabetic population, while the proliferative stage occurs more often in the juvenile diabetic population.

The (c) proliferative stage is recognized by the presence of neovascular vessels and subsequent vitreous hemorrhages. Eventually retinal detachment occurs leading to complete blindness.

Taylor and Dobree have shown that neovascular tissue arises most commonly, on retinal venules in the posterior pole of the eye (6). The next most common location is immediately on the optic disc. Proliferative lesions are rarely found directly in the macular area.

This proliferative stage is subdivided in the following way:

1. Neovascularization at the surface of the retina.
2. Neovascularization above the surface of the retina (into the vitreous).
3. Neovascularization at the optic disc.

Different visual prognosis between the non-proliferative and the proliferative stages

If diabetes is diagnosed below the age of 60, only 3 percent of the patients will be blind in the next 5 years, when non-proliferative retinopathy alone existed at the beginning of the 5-year period.

The presence of proliferative changes such as neovascularization, signifies a considerably worse prognosis. For juvenile diabetics below the age of 20, for example, 30-40 percent on the average will be blind within 5 years if proliferative diabetic retinopathy had been present at the beginning of the 5-year period. Another phenomenon, "regression" has been observed in 10 percent of patients having neovascular tissue (7).

Photocoagulation Treatment

Most investigators prefer to apply photocoagulation as soon as the patient has progressed into the proliferative stage. The photocoagulation is aimed at the neovascular vessels. It is important to start the treatment before the newly formed vessels have grown into the vitreous cavity (9).

The xenon-arc photocoagulation is used throughout the world for the last 13 years and was developed in West Germany (8). At present, it is used not only to obliterate new vessels but also to destroy normal retinal tissue in an attempt to reduce the total metabolism of the retina. Since it is believed that neovascularization of vessels is due to ischemia, reducing the

metabolic demands will, theoretically diminish the stimulus for neovascularization (10, 11).

Just within the last two years argon laser photocoagulator has become available (12). It is now possible to destroy the new vessels located at the optic disc and those spreading into the vitreous. This is possible due to the fact that the pure green light of the argon laser is predominantly absorbed by blood vessels. Time will tell whether eliminating the vessels at the optic disc and vitreous will prevent blindness in a significant percentage of these patients.

Summary

In summary, we have described the natural development of diabetic retinopathy, its classification, visual prognosis and treatment using photocoagulation.

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LAS ENFERMEDADES RESPIRATORIAS EN PUERTO RICO — PROBLEMA ACTUAL

Waldemar E. Santiago, MD

Tenemos aún problema con la Tuberculosis? Mi contestación es definitivamente sí, tenemos problema todavía en el control de la Tuberculosis en Puerto Rico. Aunque hace diez años se informaban 1,600 casos nuevos de tuberculosis en la isla, las últimas estadísticas de 1970 revelaron que el número de casos nuevos bajó a unos 800 anuales. A pesar de este logro tenemos aún problemas y estos problemas yo los divido en dos áreas:

Problemas con los casos de tuberculosis activa: El problema básico con los pacientes con tuberculosis activa consiste en que muchos son más complicados y difíciles de manejar. Tenemos actualmente en el Hospital Dr. A. Ruiz Soler un grupo de unos 40 enfermos con tuberculosis debido a bacilos poliresistentes. Este es un grupo de difícilísimo manejo debido a la poliresistencia a las drogas antituberculosas y a la dificultad de mantenerlos hospitalizados para evitar el contagio fuera del hospital de otras personas con bacilos poliresistentes.

Problemas con personas que dan una reacción positiva a la prueba de tuberculina: Se estima que en Puerto Rico hay aproximadamente un millón de personas que reaccionan positivamente a la prueba de tuberculina, lo que quiere decir que este gran grupo de personas ha estado infectado por el bacilo de la tuberculosis. En los Estados Unidos se calcula que hay veinticinco millones de personas que reaccionarían positivamente a la prueba de tuberculina. Dentro de estos dos grandes grupos están los casos activos de mañana y no tenemos en nuestro armamentario médico un método cien por ciento eficaz para evitar que estas personas desarrollen tuberculosis activa. Hay dos maneras. Un método es la inmunoprofilaxis, y el otro método la quimioprofilaxis. En el campo de la inmunoprofilaxis necesitamos primero una vacuna efectiva para uso general que protegiese a estas personas contra la tuberculosis activa. Lamentablemente esta vacuna aún no existe a pesar de

investigaciones en varios centros médicos para perfeccionarla.

En el campo de la quimioprofilaxis se usa la Isoniacida para personas que han estado en contacto con casos activos de Tuberculosis. La Isoniacida es una droga muy efectiva, barata y bien tolerada, pero desafortunadamente últimamente la literatura médica ha informado de varios casos de reacciones tóxicas a la administración de la Isoniacida. Sería altamente deseable desarrollar varias drogas para quimioprofilaxis que sustituyan la Isoniacida si es necesario.

Pasando a las enfermedades respiratorias no tuberculosas, la primera pregunta que surge es ¿Cuál es su magnitud? El censo de 1970 revela que en Puerto Rico hubo un aumento poblacional en personas de 45 años a 64 años de edad mayor de 100,000 y que hubo un aumento poblacional en personas mayores de 65 también mayor de 100,000. O sea que en el grupo de mayores de 45 años hemos tenido un aumento poblacional mayor de 200,000. Es de conocimiento general que según aumenta la longevidad, las enfermedades cardiovasculares aumentan, y hoy día las enfermedades cardiovasculares constituyen la causa número uno de mortalidad. Podemos deducir que el aumento poblacional en personas mayores de 45 años conllevará un aumento en morbilidad pulmonar.

Las enfermedades respiratorias crónicas principales son la enfisema, la bronquitis crónica y el asma bronquial. Estas enfermedades son progresivas hasta producir la incapacidad total del enfermo. El número de reclamaciones por incapacidad al Seguro Social Federal debido a enfisema ha tenido un aumento espectacular en los últimos años. El problema en el control de estas enfermedades pulmonares crónicas lo podemos dividir en dos fases: la preventiva y la terapéutica. Sabemos que el fumar afecta grandemente la predisposición para desarrollar estas enfermedades. Realmente no sabemos que sucede ni cuales son los cambios intracelulares por el humo del cigarrillo, pero sí sabemos que afecta al mecanismo de limpieza bronco-pulmonar, empezando por los macrófagos y las cilias de la mucosa bronco-pulmonar. Se ha comprobado que el humo del

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cigarrillo limita la capacidad de los macrófagos para eliminar partículas extrañas del árbol traqueo-bronquial y que así mismo el humo del cigarrillo paraliza el movimiento ciliar de las células bronco-pulmonares necesario para la limpieza natural del árbol traqueo-bronquial.

En cuanto al manejo de personas afectadas con estas enfermedades se sabe que la higiene bronquial, los ejercicios respiratorios, bronco-dilatadores, antibióticos y la terapia de inhalación son medios efectivos para mantener a estos enfermos fuera de los hospitales y mantenerlos productivos. Está probado que un paciente ambulatorio se beneficia grandemente con tratamiento de terapia de inhalación la cual debe comenzarse temprano, antes de incapacitarse el paciente. La clave del éxito terapéutico descansa en un diagnóstico temprano y tratamiento respiratorio agresivo.

Otra enfermedad que está en escala ascendente es el cáncer pulmonar. Se calcula en Estados Unidos en el

1971 hubo 60,000 muertes debido a esta enfermedad. Se ha probado que una persona que se fuma dos cajetillas de cigarrillos diarios tiene veinte veces mayores probabilidades de desarrollar cáncer en el pulmón que una persona que no fuma. El problema principal de esta enfermedad es que en la mayoría de los casos al comprobarse el diagnóstico la enfermedad ya es inoperable.

En resumen vemos como aún tenemos grandes problemas que superar en el control y manejo de la tuberculosis y en el manejo de las enfermedades respiratorias crónicas. También tenemos un enorme problema en cuanto al cáncer pulmonar donde un diagnóstico temprano salvaría a muchos de estos enfermos y la prevención a incontables más. Tenemos por frente grandes problemas que requieren solución, por lo tanto, yo exhorto a todos los médicos de Puerto Rico a una rededicación total para combatir las enfermedades de las vías respiratorias en Puerto Rico.

LA GASTRITIS MICROPOLIPOSA POTENCIALIDAD NEOPLASICA

A. Rodríguez Olleros, MD, FACP, FACC

J. E. Taveras, MD, FACP

Los trabajos de Henning (1), Heinkel (2) y Frick (3) basados en más de 5 mil pacientes con trastornos gástricos, con estudios radiográficos, gastroscopia, jugo gástrico fraccionado y biopsia gástrica, han desvalorizado el concepto clásico de la importancia de los pliegues hiperrugosos y con diferencias en su grosor en el diagnóstico de las gastritis. Encomian por el contrario el estudio del dibujo en las áreas de la mucosa o sea, las zonas de la superficie gástrica entre los pliegues y asocian sus observaciones con el resultado de las biopsias y jugo gástrico.

En observaciones gastroscópicas (6) habíamos observado casos de gastritis atróficas con mucosa blancuzca o grisácea con pliegues gruesos que dejaba transparentar vasos finos, tuberosos, que persistían aún durante la insuflación intensa. Interpretábamos estos pliegues como secuelas de un proceso gástrico antiguo con proliferación "conectiva" submucosa e hipertrofia de la muscularis mucosa.

Aoyama (4) participa también del criterio de poner atención principalmente en el estudio de ciertas áreas de la mucosa para el diagnóstico de las gastritis. Indica que el encontrar áreas de la mucosa de más de 1 mm. de espesor y de diferentes tamaños es muy probable que se trate de gastritis atrófica "hiperplásica".

Otro autor, Cheli, (5) afirma que la gastritis atrófica "hiperplásica" asocia la atrofia glandular a una hiperplasia de la zona superficial formando vellosidades irregulares pseudopoliposas.

Pacientes y Métodos

(Fig. 1) Presentamos ocho pacientes de gastritis atrófica micropoliposa comprobada por biopsias gástricas del antro y del cuerpo tomadas bajo control del cinefluoroscopio. Siete de los pacientes tenían más de 60 años y el octavo tenía 78 años.

De la Universidad de Puerto Rico, Facultad de Farmacia y Facultad de Medicina; del Hospital Ruiz Soler, Depto. de Salud de Puerto Rico. Leído en la Convención AMPR - Noviembre de 1971.

Siete eran mujeres y uno hombre. Todos habían tenido síntomas gástricos desde hacía 10 a 15 años. En la mayoría se habían iniciado los síntomas al tomar analgésicos. El examen fraccionado del jugo gástrico había evidenciado aclorhidria en todos los casos con dosis máxima de Histalog de 50 mlg.

El hombre había sido operado de gastrectomía por úlcera duodenal hacía 16 años y tres mujeres habían sufrido colecistectomía por calculosis.

En estos cuatro pacientes y en una paciente adicional se comprobó reflujo duodenal en el contenido residual gástrico. Seis de nuestros pacientes fueron estudiados clínicamente. Los dos restantes son observaciones quirúrgicas, pero nos consta que el examen del jugo gástrico previo a la operación evidenció aquilia gástrica por el método fraccionado con estímulo de Histalog.

El dibujo radiológico de las áreas de mucosa en los ocho pacientes era sugestivo de gastritis micropoliposa por su forma granular o poligonal en panal de abeja. (Fig. 2, 3, 4).

En tres pacientes que fueron examinados con el gastrofibroscopio, cuando se les sometía a mediana distensión del estómago el cuerpo gástrico presentaba una imagen de mucosa atrófica en mosaico: *figura de mucosa grisácea pálida con un centro rosado rojizo*.

Siete pacientes tenían en las biopsias, atrofia, metaplasia intestinal y micropoliposis. Una paciente tenía atrofia sin metaplasia, pero se apreciaba micropoliposis. (Fig. 5, 6, 7, 8).

Tres de nuestros pacientes han sido operados. Dos corresponden a las observaciones quirúrgicas a las que se llegó por diagnóstico radiológico. Los dos son tumores benignos: leiomioma y pólipo adenomatoso. Ambos tenían el resto de la mucosa gástrica atrófica con metaplasia intestinal y micropoliposis.

El tercer operado es una enferma de observación clínica en la que incluso dos buenos estudios de un radiólogo solamente había evidenciado áreas poligonales en la mucosa. El examen del jugo gástrico demostraba aquilia. La biopsia demostró atrofia metaplasia y micropoliposis. El cirujano cancerólogo operó con el propósito de extirpar la zona afectada de micropoliposis del antro y cuerpo gástrico, pero encontró además un tumor carcinomatoso pequeño en el fornix gástrico.

Comentarios

Konjetzny (7) ha sido la histórica figura que sugiere que el cáncer gástrico es con gran frecuencia un proceso subsiguiente a la gastritis crónica atrófica. Este autor planteó el problema en la conciencia de la gastroenterología.

Paciente	Edad	Sexo	Antecedentes	Apariencia de Mucosa a Rayos X:	Biopsia Gástrica X Selectiva	Reflujo de Bilis	Neoplasma:
A. R.	Más de 60	M	Gastrectomía Gastritis atrof. por más de 10 años	Areas irregulares 3mm. o más	Atrofia mucosa Metaplasia Intest. Micropoliposis	Presente	
G. R.	Más de 60	F	Colecistectomía Gast. Atrof. más de 10 años.	Areas irreg. de 3mm. o más.	Atrofia mucosa Metaplasia Intest. Micropoliposis.	Presente	
R. R.	Más de 60	F	Colecistectomía Gastritis Atrof. más de 10 años	Imagen en Panal	Atrofia mucosa Metaplasia Intest. Micropoliposis	Presente	Ca. Gástrico
S. F.	Más de 60	F	Colecistectomía Gastritis Atrof. más de 10 años	Areas granulares 3mm. o mayores	Atrofia mucosa Metaplasia Int. Micropoliposis	Presente	
L. E.	Más de 60	F	Gastritis Atrof. más de 10 años	Areas irregulares granulados	Atrofia mucosa Metaplasia Int. Micropoliposis		
A. R. R.	Más de 60	F	Gastritis Atrof. más de 10 años	Areas de granularidad regulares	Atrofia mucosa Metaplasia Intest. Micropoliposis		Leiomioma Gástrico
O. R. A.	Más de 60	F	Gastritis Atrof. Más de 10 años	Apariencia en panal	Atrofia mucosa Micropoliposis	Presente	
M. S. R.	Más de 70	F	Gastritis Atrof. Más de 10 años	Areas granulares de 3mm o mayores	Atrofia mucosa Metaplasia Intest.		Adenoma Gástrico

Figura 1



Fig. 2: Imagen radiográfica mostrando áreas de superficie de mucosa irregular.

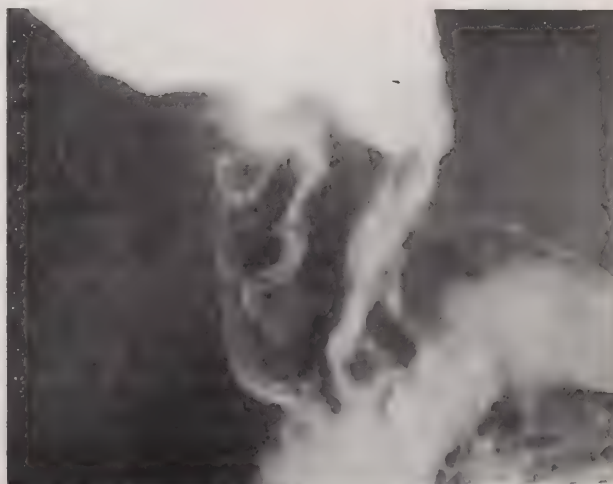


Fig. 3: Imagen de la superficie de la mucosa con la apariencia que llamamos granular.



Fig. 4: Imagen en forma reticulada que hemos llamado en panal de abejas.

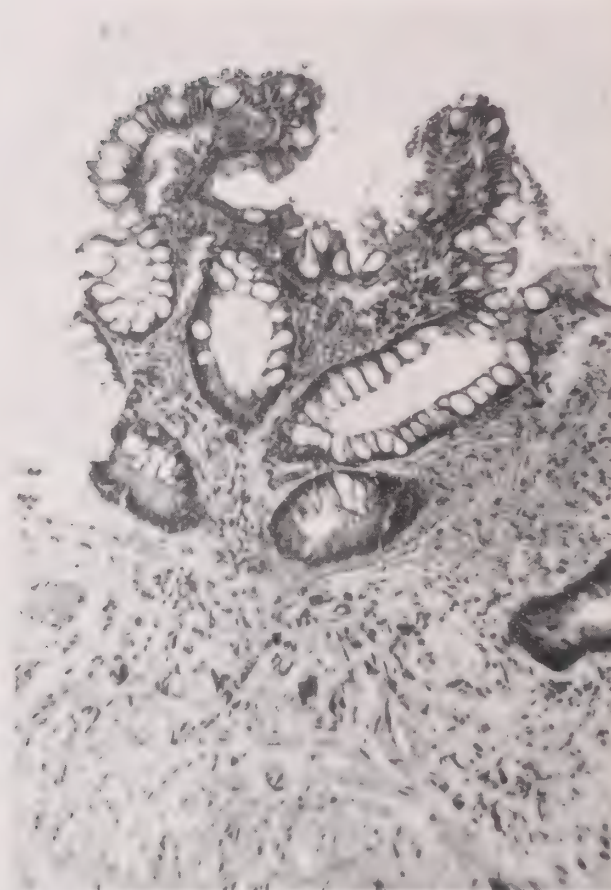


Fig. 5: Caso de gastritis atrófica severa con micropoliposis y metaplasia intestinal. El estroma se ve infiltrado por linfocitos y células plasmáticas. Nótese la prominencia de la muscularis mucosae.

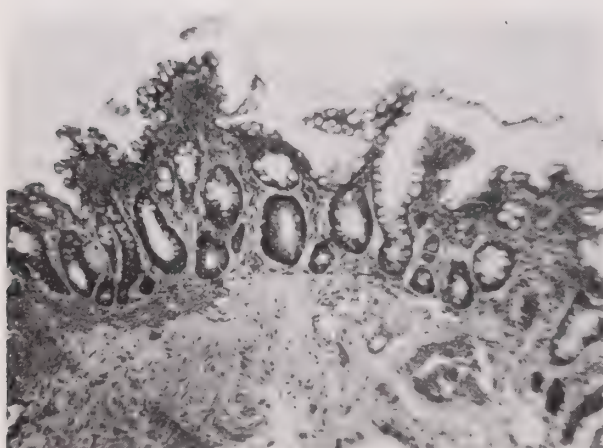


Fig. 6: Gastritis atrófica con metaplasia intestinal. Nótese la micropoliposis irregularmente repartida en la superficie.

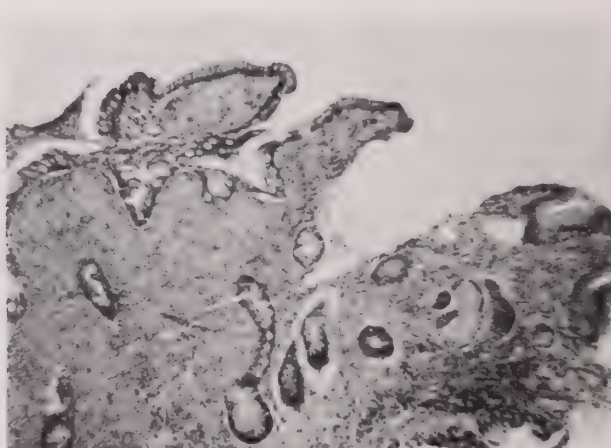


Fig. 7: Otro caso de gastritis atrófica con micropoliposis. Nótese la escasez de glándulas gástricas.

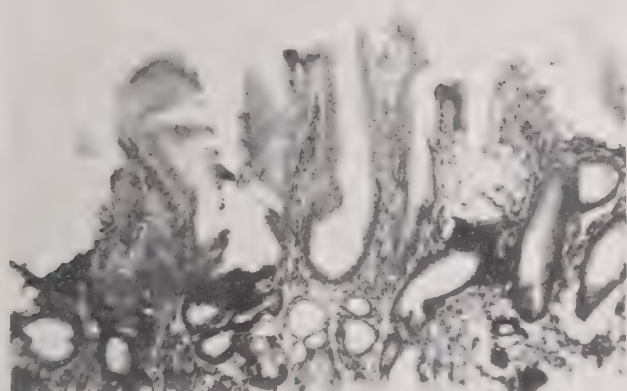


Fig. 8: Mucosa gástrica adyacente a un adenoma. Véase la metaplasia intestinal y formación micropoliposa. Algunas glándulas forman microquistes.

En 1955 Morson (8, 9) publica sus trabajos sugiriendo relación entre metaplasia intestinal y cáncer gástrico. Cita, participando de él, el concepto defendido por Magnus: "la presencia de un epitelio intestinal en el estómago es el resultado de regeneración perturbada del epitelio de una superficie en una mucosa repetidamente lesionada por gastritis y es un ejemplo de metaplasia resultante de irritación crónica".

Hitchcock (10) en un examen cuidadoso de 1399 aclorhídricos encuentra 47 casos de pólipos gástricos y 13 de cáncer.

En el Cancer Detection Center de la Universidad de Minnesota se seleccionaron 1769 personas con aclorhidria siguiéndolas durante 7 años encontrando que la frecuencia de cáncer de estómago en ellos era 5.2 veces más que en el grupo de edad similar en la población general.

Elster (11) encuentra 43 por ciento de metaplasia en las úlceras duodenales, 80 por ciento en las úlceras gástricas y 77 por ciento en el carcinoma gástrico. Cree que la metaplasia es consecuencia de la inflamación crónica, pero no relaciona la metaplasia con el cáncer gástrico.

Valencia Parpacén (12) de su extenso material de biopsias gástricas deduce dos tipos de gastritis atróficas: uno con infiltración y poca probabilidad de metaplasia y el otro de gastritis atrófica sin infiltración y en las que más frecuentemente coexiste la metaplasia intestinal.

No debemos olvidar que una atrofia con infiltración de células mononucleares sugiere una gastritis por

autosensibilización probablemente en sus primeros tiempos.

Se han realizado estudios enzimáticos en las células de metaplasia intestinal del estómago. Planteydt (13) encuentra en su estudio alta actividad de aminopeptidasa en un 50 por ciento de los carcinomas gástricos y una análoga proporción e intensidad la encuentra en la metaplasia intestinal de la mucosa gástrica.

Un grupo de autores checos, (14) encuentra aumento de esterasa en las células metaplásicas al igual que en las tumorales teniendo además ambos tejidos la presencia de aminopeptidasa y fosfatasa alcalina.

De los anteriores estudios no se deduce ninguna conclusión, pero puede afirmarse que son análogas las desviaciones de los enzimas investigados en las células cancerosas. Esta analogía refuerza la hipótesis de Morson.

¿Por qué se origina la metaplasia en las gastritis crónicas atróficas? Se ha atribuido al factor injuriante del reflujo duodenal. Rhodes (15) encuentra mayor reflujo biliar en el estómago de baja acidez. Además, el jugo ácido precipita los ácidos biliares en tanto que en el jugo anácido la bilirrubina en solución es más concentrada y más injuriante.

En análogo sentido se habían expresado Du Plessis (16) Capper (17) y Cole (18). Lawson (19) derivando con fístula la bilis y jugo pancreático al estómago de perros obtiene a los 200 días gastritis atróficas con proliferación del epitelio superficial formando papilas y con un aumento considerable de las mitosis celulares.

Taylor (20) afirma que la mucosa gástrica con metaplasia intestinal es capaz de absorber grasas y deduce de ello la posibilidad de absorción de los agentes carcinogénicos solubles en las grasas.

Comprobando lo anterior Sivrala (21) administra trioleína emulsificada, triglicéridos de cadenas medianas y ácido oléico libre a 30 pacientes en los cuales 12 tienen metaplasia difusa de la mucosa del cuerpo gástrico. Obtiene biopsias previas a la administración de los lípidos y las vuelve a practicar a los 30 y 60 minutos y a las 24 horas después de administrarlos. Comprueba que las células de metaplasia intestinal absorben los glicéridos de cadenas medianas y el ácido oléico.

Hay unos trabajos muy interesantes y en favor del criterio de Konjetzny (7) realizados por el grupo de investigadores dirigidos por Sivrala (22, 23, 24). Examinan con biopsias en cuerpo gástrico a una comunidad rural. Encuentran gastritis en el 53 por ciento de las personas que oscilan entre los 16 y 60 años de edad. La gastritis superficial corresponde al 25 por ciento y la atrófica al 28 por ciento. La gastritis atrófica

aumenta con la edad en tanto que la gastritis superficial es común en todas las edades. El tiempo necesario para la transición de una gastritis superficial a una atrófica lo estiman en 9 años.

Este y otros trabajos con examen de biopsias seguido por un largo período revela a los autores que la gastritis atrófica se desarrolla a partir de una gastritis superficial. En otra investigación 100 pacientes de gastritis atrófica fueron reexaminados 10-15 años más tarde y por segunda vez 5-8 años después de la primera revisión. Dos pacientes habían muerto de cáncer gástrico antes de la primera revisión. A uno se le evidenció cáncer en la primera revisión. En la segunda y última revisión se encuentran dos casos de pólipos y 6 de carcinoma gástrico.

Paralelamente se revisaron 93 pacientes con gastritis superficial y 168 que tenían mucosa normal. Ninguno de estos grupos desarrollaron cáncer en el mismo período.

En los 8 casos presentados en este trabajo se iniciaron clínicamente las alteraciones gástricas por causas medicamentosas irritantes (aspirinas, etc.) instaurándose después de la gastritis atrófica. Recordemos que del 60 por ciento de las gastritis superficiales desarrollan anticuerpos visceros específicos frente a las células parietales. (25, 26, 27).

En los casos en quienes practicamos cateterismo gástrico se comprobó la presencia del reflujo duodenal en el contenido gástrico.

En conclusión: sobre la mucosa gástrica de nuestros ocho pacientes han estado gravitando las condiciones que el sentido pavloviano de la biología adscribe al desarrollo de tumores (28) "se consideran los tumores como reacciones proliferativas de partes del organismo reaccionando a varios factores nocivos, extrínsecos o intrínsecos que de manera consistente perturban la composición y estructura de los tejidos y células y alteran su metabolismo"

Resumen

Se presentan ocho pacientes geriátricos con micropoliposis gástrica. Todos habían padecido gastritis atrófica por varios años. El dibujo radiológico de la micromucosa levantó la sospecha de las lesiones. En cinco de los ocho pacientes se comprobó reflujo duodenal.

En siete la micropoliposis coexistía con metaplasia intestinal intensa. En tres de estos pacientes se ha comprobado quirúrgicamente la existencia de los siguientes tumores: carcinoma gástrico, leiomioma y

pólipo adenomatoso.

Summary

Eight geriatric patients with micropolyposis are presented. All had suffered with severe atrophic gastritis for years.

The radiologic pattern of the micromucosa provided the clue to the diagnosis.

Five showed duodenal reflux. Seven showed coexistent intestinal metaplasia. Three patients were explored surgically and the presence of the following tumors was established: gastric carcinoma, leiomyoma and adenomatous polyp.

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ASPECTOS MEDICO-LEGALES

SALE OR DISPOSITION OF A MEDICAL PRACTICE

(Prepared by The Office of the General Counsel of the American Medical Association)

THE OFFICE LEASE

The office lease contains a continuing obligation to pay the amount of the rent to the end of the term of the lease. It likewise contains a continuing right to occupy the premises to the end of the term. When the practice is sold, the purchaser will normally view the office lease as part of the goodwill. We will have further reference to this below. If the unexpired term of the lease is fairly substantial, an assignment or sublease may be indicated. It should be noted that most leases provide for an assignment or sublease only with the written consent of the landlord. Also, it should be noted that the landlord's consent to an assignment or sublease does not release the original tenant (or his estate) from liability under the lease. It simply means that the landlord now has the original tenant and the sub-tenant both responsible for the lease. If the sub-tenant defaults in the payment of the rent, the original tenant is in the position of a guarantor. Accordingly, when the medical practice is sold and the purchaser is going to take over the same office space, every effort should be made to obtain a release from the landlord in addition to his consent to a sublease or assignment. This is also important when the unexpired term of the lease is very short, assuming this lease is not particularly desirable to the purchaser since he will have to negotiate for an extension of the term or a new lease in the near future. If the purchaser has to move his office to another location, he will be unwilling to pay as high a price for the purchase of the practice. This is frequently the case where the doctor's practice has been conducted out of the residence rather than in a rented office. So it may be important in the sale of a practice to be able to promise the purchaser that the landlord will give him a completely new lease for a designated term. The purchaser will be looking for a term which is long enough to provide him with some stability, yet not too long to prevent him from making needed changes and adjustments in his practice.

It is not unusual for a physician to make certain improvements to the leased space for his convenience and to increase his efficiency. These might include a variety of built-in cabinets and utilities. It should be noted that, for the most part, these improvements become the property of the landlord and the tenant cannot remove them without the landlord's consent.

GOODWILL

Goodwill is the intangible value of an actual operating business. In the sale of a medical practice, it is the opportunity of serving the patients of the physician who is selling his practice. It is based on the probability that some of the patients will elect to be treated by the physician who has purchased the prac-

tice. No one can guarantee that any patient will do so, but it can be conceded that many of them will. They will return to the old familiar office, hence the importance of the lease becomes more apparent, or they will dial the well-memorized telephone number of the former physician.

Placing a dollar and cents figure upon the goodwill of a practice being sold is most difficult, and is not unaffected by tax considerations. Although it is not too significant to the seller who will have to pay capital gains taxes on the amount of profit attributable to goodwill, the amount paid for goodwill is a capital asset to the buyer which cannot be depreciated. The buyer can recapture the tax advantage only by a subsequent sale of the same practice. Since no doctor anticipates selling a practice which he has purchased, at least for many years, the buyer is anxious to keep the amount attributable to goodwill at a minimum. However, he may be willing to pay a higher price for the physical assets which he can depreciate for tax purposes.

The doctor who is retiring faces an additional problem in this area. When he enters into a contract for the sale of his practice, the buyer may want two particular provisions for his own benefit. First, he may want the selling physician to agree to assist him, or at least make himself available for consultation with the purchasing physician for a designated period of time after the sale. This is a customary provision, and the purpose is to assist the physician in taking over the practice. Second, the purchasing physician may want a "Covenant Not to Compete". That is, the purchasing physician does not want the selling doctor to open an office down the street in competition with him. If the seller were permitted to do so, he would undoubtedly keep all of his patients, and the purchaser would actually acquire no "goodwill". To correct this problem, the law permits the parties to the sale of a business to agree in their contract that the seller will not engage in the same type of business for a reasonable period of time after the sale, within the same area served by the business operation being sold. Normally, this type of provision is important to the buyer of a medical practice because of the personal nature of the practice.

This "Covenant Not to Compete", by itself, is clearly intended to assist the purchaser in acquiring the goodwill of the practice and, therefore, any dollar amount attributable to this covenant would be handled for tax purposes as indicated above, generally to the buyer's disadvantage. The problem arises when the two provisions (i.e., to assist the buyer and not to compete) are construed together and no consideration is attached to the seller's obligation to assist the purchaser. The Internal Revenue Service may construe the amount allocated as goodwill to be consultants' fees, which would be taxable as ordinary income to the seller and deductible by the purchaser. This construction may be

strengthened if the contract provides for installment payments of the purchase price, and further reinforced by draftsmanship which is designedly broad and vague.

Of course, the physician must follow the advice of his lawyer, as each transaction is separate and no general rule can be laid down to cover all types of situations, but it might

be well to specifically allocate an agreeable amount to consultation fees in addition to the amount provided for goodwill, so that the tax consequences will not be subject to speculation.

(To be continued)

GRAVE PROBLEMA DE LA RETINOPATIA DIABETICA

Desde el hallazgo fortuito de la insulina, mayor número de diabéticos viven lo suficiente para desarrollar complicaciones vasculares, incluyendo la retinopatía diabética. Esta se constituye ahora en una de las causas más frecuentes de ceguera.

La diabetes es una enfermedad común que afecta el 1.7 por ciento de la población del mundo occidental. Existe también una gran reserva de pacientes sin diagnosticar, con una prevalencia verdadera de alrededor de 4 por ciento. Afecta a las mujeres más frecuentemente que a los hombres en una relación de 3 a 2. Un historial familiar de diabetes aparece en cerca de 25 por ciento de los pacientes. La transmisión de la enfermedad se inclina hacia un rasgo recesivo.

La retinopatía diabética se desarrolla en el 50 por ciento de los diabéticos. Sin embargo, si la enfermedad ha estado presente por más de 18 años, el 90 por ciento tendrán retinopatía.

Esta enfermedad ocupa el tercer lugar entre las causas más frecuentes de ceguera en los Estados Unidos. En la actualidad hay alrededor de 155,000 personas ciegas por causa de la diabetes pero se predice que para el año 2,000 ese número ascenderá a medio millón en los Estados Unidos, un número mayor que el total de ciegos por todas las causas al presente. Esta predicción se basa en un aumento de 9 por ciento anual en el número de diabéticos en los Estados Unidos, por ciento que ha persistido desde el 1958.

¿Cómo se desarrolla la retinopatía diabética? Ocurren cambios en las capilares que impiden la utilización adecuada del oxígeno por la retina, la cual, en un intento compensatorio por obtener el oxígeno que le falta, forma nuevos vasos sanguíneos a manera de una enredadera.

Desgraciadamente estos nuevos vasos sanguíneos son altamente frágiles y sus paredes se rompen con mucha facilidad produciendo hemorragias intraoculares frecuentes.

La sangre vertida en la cámara posterior del ojo daña el humor vítreo que allí se encuentra por el contenido de hierro de la hemoglobina. Una vez sufre daño la gelatina o humor vítreo, bandas glióticas en la cavidad del vítreo halan la retina y la arrugan quedando el paciente totalmente ciego.

¿Contamos con algún tratamiento efectivo para combatir la retinopatía diabética?

Ningún intento terapéutico es completamente satisfactorio pero lo más aceptado en la actualidad es la fotocoagulación, la cual se usa para destruir los nuevos vasos en la retina tan pronto se detectan éstos en el paciente diabético. Con este método se enfoca un rayo de luz bien intenso a través de la pupila del enfermo para literalmente quemar los vasos recién formados. De esta manera se evitan las hemorragias intraoculares.

Actualmente usamos el rayo laser de argon, que por ser de color verde puede destruir selectivamente los vasos sanguíneos neoformados de color rojo.

¿Cuál es el problema mayor con que se enfrenta el oftalmólogo al tratar de evitar la ceguera en estos pacientes?

Muy frecuentemente vemos al diabético por primera vez con una retinopatía diabética avanzada la cual ya no puede ser tratada. Una vez la retina ha sido damnificada por las bandas glióticas que se han formado, ningún tratamiento es efectivo.

Afortunadamente, la retina es accesible fácilmente a inspección periódica. La única forma de prevenir la ceguera en pacientes diabéticos, depende pues, del examen frecuente del paciente y una decisión juiciosa y temprana de apelar a la fotocoagulación cuando puede tratarse al diabético.

José A. Berrocal, MD

SOBRE LA PUBLICACION DE TRABAJOS EN IDIOMA INGLES (WHY ARE WE PUBLISHING IN ENGLISH?)

Los Editores de esta revista han sido criticados por publicar en idioma inglés algunos de sus trabajos.

Se nos ha dicho que siendo una revista latinoamericana debería publicarse solamente en Castellano o Portugués, y que los lectores extranjeros que no entiendan nuestro idioma deberían conseguir una traducción de los mismos.

Otra de las críticas está teñida de un matiz ideológico. Se ha dicho que esto demuestra una actitud de sometimiento intelectual a países de habla inglesa sobre todo a Estados Unidos. En el Núm. 1 de Acta, en la Presentación habíamos expresado que queríamos una publicación con difusión mundial y que por esa razón además de los idiomas vernáculos publicaríamos en inglés y francés. Es un hecho conocido por todos, que el inglés es el más difundido de los idiomas para trabajos científicos del tipo de los que se publican en Acta. Los lectores no son solamente de habla inglesa sino que pueden ser europeos, asiáticos, africanos, etc., es decir aquellos a los cuales queremos difundir nuestros trabajos para obtener un intercambio científico. Esta es la realidad que hemos contemplado. Numerosas publicaciones de origen no inglés han adoptado el mismo sistema, por ejemplo la gran mayoría de trabajos Escandinavos. Algunos países con gran tradición científica como Alemania y Francia aparecen en numerosas publicaciones trabajos en inglés. En nuestro país ya lo hacen Revistas de prestigio como Medicina y Acta Fisiológica Latinoamericana.

Tener la pretensión de obligar a nuestros lectores extranjeros a aprender el español sería una gran ingenuidad.

La razón expuesta es la única que nos lleva a publicar los trabajos en inglés. Dar la connotación de sometimiento intelectual a este hecho, es caer en confusión y derivar conflictos de ideología a una publicación estrictamente científica.

LOS EDITORES (Reproducido con permiso del Acta Gastroenterológica Latinoamericana, edición Vol. 3, No. 4, octubre-diciembre 1972)

CARTA AL EDITOR

Jorge O. Just Viera, MD., Editor
Boletín de la Asociación Médica de P. R.,
Fernández Juncos 1305, P. O. Box 9387
Santurce, Puerto Rico 00908

Dear Dr. Just-Viera:

The World Medical Association is co-sponsoring a world Conference on the Human Environment, October 23-26, 1973, in Primosten, Yugoslavia, in collaboration with the Union of Yugoslav Medical Societies, the American Medical Association and the United States Department of Health, Education and Welfare.

This conference will cover not only pollution, but the effects of urbanization, housing, waste disposal, water supply, nutrition, radiation and other factors on humans. The responsibilities of the medical and allied medical professions in improving the environment in developed and developing countries will be emphasized on the final day of the conference.

This meeting is a follow up on the United Nations Stockholm meeting of June 1972, but because it will be attended by members of the Eastern block (iron curtain) countries who were absent from the earlier meeting for political reasons, it should have a greater

impact on international understanding and good will.

There is no registration fee and board and lodging will be under \$10 a day. Registration blanks can be obtained from The World Medical Association or from Mr. Frank Barton, Council on Environment and Public Health of the American Medical Association.

If any of your readers are interested in associate membership (\$15 a year) in The World Medical Association which, made up of 58 national medical associations, sets ethical standards for the private practice in medicine worldwide and has sponsored four international conferences on medical education, they can apply to The World Medical Association, 10 Columbus Circle, New York, N. Y. 10019. The next annual Assembly will be in Munich, Germany, October 14-20, 1973 just prior to the Primosten conference and will include the 100th Anniversary of the Bundesaerztekammer - the German Medical Association and a two-day session on the computer in medicine and the confidentiality of information between patient and physician.

Sincerely yours,
(Sgd) Gerald D. Dorman, MD
Executive Director, Finance

NOTICIAS

ASOCIACION PUERTORRIQUEÑA DEL CORAZON - SE- SION CIENTIFICA ANUAL

Septiembre 22 y 23 de 1973 - Hotel Caribe Hilton, San Juan, Puerto Rico

ABSTRACTOS

El Comité Científico invita a enviar abstractos de trabajo originales para considerarse para la Convención Anual que se llevará a cabo el 22 y 23 de septiembre de 1973 en San Juan.

Procedimiento:

1. Enviar un abstracto de 250 palabras o menos en maquina a doble espacio. Se necesitarán un original y tres copias.
2. Adjuntar en una tarjeta de 3 x 5 con los siguientes datos, en el siguiente orden:
 - a) Autor principal y su dirección.
 - b) Autor que hará la presentación.
 - c) Autores colaboradores.
 - d) Título del trabajo.
 - e) Institución del estudio, ciudad.
 - f) Equipo audiovisual que se requiere para la presentación.
3. Enviar lo anterior a: Amalia Martínez Picó, MD, Presidente del Comité Organizador, Asociación Puertorriqueña del Corazón - Apartado 8215, Fernández Juncos, Santurce, Puerto Rico 00910.

LA FECHA FINAL PARA RECIBIR LOS ABSTRACTOS ES JULIO 15 DE 1973.

Exhibiciones Científicas:

Las solicitudes para exhibiciones científicas serán bienvenidas por el Comité Científico, debiendo enviarse éstas a la persona anteriormente mencionada, antes de julio 15 de 1973. (Favor adjuntar una descripción detallada del mismo y el espacio necesario para su presentación).

The forthcoming annual meeting of the American Association for Clinical Immunology and Allergy will be held at The Hilton Palacio Del Río Hotel, San Antonio, Texas, November 29-December 2, 1973.

Please direct inquiries to our Program Chairman: Robert J. Brennan, MD, President-Elect American Association for Clinical Immunology & Allergy, 3471 N. Federal Hwy., Ft. Lauderdale, Fla. 33306.

Annual Clinical Meeting: American College of Obstetricians and Gynecologists. May 21-24, Americana Hotel, Bal Harbour, Fla. This 21st annual clinical meeting will feature formal papers, reports on current investigations, and specialty meetings on Community Health, Maternal and Perinatal Medicine, Oncology, Pediatric and Adolescent gynecology, and Psychosomatic

Obstetrics and Gynecology. There will be two "Great Debates", breakfast conferences and a full motion picture program. New this year are postgraduate courses throughout the meeting as well as preceding it, and informal Curbstone Consultations with two authorities on each subject. New Self-Assessment Tests in Clinical Obstetrics and Clinical Gynecology. Registration fee for nonmembers, \$125.

Contact: Donald F. Richardson, Associate Director, American College of Obstetricians and Gynecologists, One East Wacker Drive, Chicago, Ill. 60601.

The American Board of Family Practice announces that it will give its next two-day written certification examination on October 20-21, 1973 in various centers throughout the United States. Information regarding the examination can be obtained by writing:

Nicholas J. Pisacano, MD, Secretary
American Board of Family Practice, Inc.
University of Kentucky Medical Center
Annex No. 2, Room 229
Lexington, Kentucky 40506

PLEASE NOTE: It is necessary for each physician desiring to take the examination to file a completed application with the Board office. *Deadline for receipt of applications in the Board office is August 1, 1973.*

ANNOUNCEMENT AND INVITATION

The Medical Service of the San Juan Veterans Administration Hospital announces a Workshop on the Problem Oriented Medical Record to be held from 9:00 am to 4:00 pm on March 14, 1973 at the Auditorium, 2nd Floor of the Hospital.

The Problem Oriented Medical Record System is a tool that enables rapid retrieval of information from the record, better self assessment, continuing medical self education and better patient care. Its adoption is currently being recommended by several review committees, specialty boards and other responsible organizations involved in hospital and training program evaluation.

The Workshop will be divided into two parts. The morning session will cover the mechanism of the System; the afternoon session will cover the implementation. The participants are from the University of P. R. Medical School and the San Juan VA Hospital. You and interested members of your staff are cordially invited to attend.

Please address all inquiries to Dr. Eli A. Ramírez, Chief, Medical Service, Veterans Administration Hospital, GPO Box 4867, San Juan, Puerto Rico 00936. Telephone: 764-4545, Ext. 311.

ARTICULOS APROBADOS

1. Doctors, Defenses and the Age of Informed Consent (Second Part) - Lou Ashe, JD, LLM
2. Cáncer del Cuello de la Matriz Entre las Mujeres de Varones con Cáncer del Pene - Isidro Martínez, MD, et al
3. Prevalence of Hepatitis-Associated Antigen (HAA) in Collagen Disorders - Mario Ravry, MD, et al
4. La Preservación Experimental y Clínica de Riñón para Trasplante - E. A. Santiago Delpín, et al

I N D I C E D E A N U N C I A N T E S

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6. *Roche Laboratories — Librium, Valium, Efudex*
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the bare facts...

Plain topical steroids alone are not primarily recommended if the skin lesion has become infected with fungi or bacteria.

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INDICATIONS

Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, the FDA has classified the indications as follows:
Possibly* effective: Contact or atopic dermatitis; impetiginized eczema; nummular eczema; infantile eczema; endogenous chronic infectious dermatitis; stasis dermatitis; pyoderma; chalcid eczema and chronic eczematoid otitis externa; acne vulgaris; localized or disseminated neurodermatitis; lichen simplex chronicus; anogenital pruritus (vulvae, scroti, ani); folliculitis; bacterial dermatoses; mycotic dermatoses such as tinea (capitis, cruris, corporis, pedis); moniliasis; intertrigo. Final classification of the less-than-effective indications requires further investigation.

CONTRAINDICATIONS

Hypersensitivity to Vioform-Hydrocortisone, or any of its ingredients or related compounds; lesions of the eye; tuberculosis of the skin; or viral skin lesions (including herpes simplex, vaccinia, and molluscum).

WARNINGS

This product is not for ophthalmic use.

In the presence of systemic infections, appropriate systemic antibiotics should be used.

Use in Pregnancy

Though topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use in pregnant females has not been established. Therefore, they should not be used extensively in pregnant patients in large amounts or for prolonged periods of

PRECAUTIONS

May prove irritating to sensitized skin in rare cases. If this occurs, discontinue therapy. May stain.

If used under occlusive dressings or for a prolonged period, watch for signs of pituitary-adrenal axis suppression.

May interfere with thyroid function tests. Wait at least one month after discontinuance of therapy before performing these tests. The ferric chloride test for phenylketonuria (PKU) can yield a false-positive result if Vioform is present in the diaper or urine.

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Few reports include: Hypersensitivity, local burning, irritation, pruritus. Discontinue if untoward reaction occurs. Rarely, topical corticosteroids may cause striae at site of application when used for long periods in intertriginous areas.

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Apply a thin layer to affected areas 3 or 4 times daily.

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Cream, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearyl alcohol, spermaceti, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of 5 and 20 Gm.
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Lotion, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearic acid, cetyl alcohol, lanolin, propylene glycol, sorbitan trioleate, polysorbate 60, triethanolamine, methylparaben, propylparaben, and perfume Flora in water; plastic squeeze bottles of 15 ml.
Mild Cream, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a water-washable base containing stearyl alcohol, spermaceti, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of 1/2 and 1 ounce.
Mild Ointment, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a petrolatum base; tubes of 1/2 and 1 ounce.

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Librium (chlordiazepoxide HCl) is used as adjunctive antianxiety therapy concomitantly with certain specific medications of other classes of drugs, such as cardiac glycosides, anti-hypertensive agents, diuretics, anticholinergics and antacids.

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Effect on mental acuity: Usually minimal on proper maintenance dosage.

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**5-mg, 10-mg, 25-mg capsules
up to 100 mg daily in
severe anxiety**

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Relief of anxiety and tension occurring alone or accompanying various disease states.

Contraindications: Patients with known hypersensitivity to the drug.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation, or in women of childbearing age requires that its potential benefits be weighed against its possible hazards.

Precautions: In the elderly and debili-

tated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the

elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage, fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

Supplied: Librium® capsules containing 5 mg, 10 mg or 25 mg chlordiazepoxide HCl. Libritabs® tablets containing 5 mg, 10 mg or 25 mg chlordiazepoxide.



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BOLETIN ASOCIACION MEDICA DE PUERTO RICO

PLAY
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Vol. 65

Marzo 1973

No.3



Everybody experiences psychic tension.



Most people can handle this tension.



Some people develop excessive psychic tension and need your counseling,



and a few may need counseling
and the psychotropic action of Valium® (diazepam).

Before deciding to make Valium (diazepam) part of your treatment plan, check on whether or not the patient is presently taking drugs and, if so, what his response has been. Along with the medical and social history, this information can help you determine initial dosage, the possibility of side effects and the ultimate prospects of success or failure.

While Valium can be a most helpful adjunct to your counseling, it should be prescribed only as long as excessive psychic tension persists and should be discontinued when you decide it has accomplished its therapeutic task. In general, when dosage guidelines are followed, Valium is well tolerated (see Dosage). For convenience it is available in 2-mg, 5-mg and 10-mg tablets.

Drowsiness, fatigue and ataxia have been the most commonly reported side effects.

Until response is determined, patients receiving Valium should be cautioned against engaging in hazardous occupations requiring complete mental alertness, such as driving or operating machinery.



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Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

Dosage: Individualize for maximum beneficial effect.

Adults: Tension, anxiety and psychoneurotic states, 2 to 10 mg b.i.d. to q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed; adjunctively in skeletal muscle spasm, 2 to 10 mg t.i.d. or q.i.d.; adjunctively in convulsive disorders, 2 to 10 mg b.i.d. to q.i.d. **Geriatric or debilitated patients:** 2 to 2½ mg, 1 or 2 times daily initially, increasing as needed and tolerated. (See Precautions.) **Children:** 1 to 2½ mg t.i.d. or q.i.d. initially, increasing as needed and tolerated (not for use under 6 months).

Supplied: Valium® (diazepam) Tablets, 2 mg, 5 mg and 10 mg; bottles of 100 and 500. All strengths also available in Tel-E-Dose® packages of 1000.

Valium® (diazepam)

To help you manage excessive psychic tension

BOLETIN

ASOCIACION MEDICA DE PUERTO RICO



Organo Oficial

Fundado en 1903

Volumen 65

Marzo 1973

Número 3

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Anuncios, Suscripciones y Reimpresos:

El Boletín se publica mensualmente. El precio de suscripción es de \$10.00 al año. Todo material de anuncio está sujeto a aprobación por la Junta Editora. La tarifa de precios para anuncios será suministrada a solicitud. Copia del anuncio debe ser recibida el día primero del mes que precede al mes de publicación. Representante de anuncios nacionales es la State Medical Journal Advt. Bureau, 1010 Lake St., Oak Park, Ill. 60301.

Podrán ordenarse reimpresos de los artículos a publicarse cuando se reciba notificación de su aceptación.

Trabajos Científicos:

El Boletín acepta para su publicación artículos relativos a medicina y cirugía y las ciencias afines. Igualmente acepta artículos especiales y correspondencia que pudiera ser de interés general para la profesión médica. El artículo, si se aceptara, será con la condición de que se publicará únicamente en esta revista. La AMPR no se hace responsable de las opiniones y declaraciones vertidas por los autores y sus puntos de vista no necesariamente representan aquellos de la AMPR; cualquier relación con la política oficial es coincidencia.

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CUBIERTA DEL MES DE MARZO:

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(Cortesía del XI Congreso Panamericano de Gastroenterología)



acute arthritic inflammation...heat that freezes

In acute rheumatoid arthritis consider Tandearil. The anti-inflammatory action of Tandearil quickly helps reduce heat, pain, swelling, and stiffness. Results are usually seen in 3 or 4 days. Try it for a week when the symptoms defy aspirin control.

Remember that Tandearil is not a simple analgesic. It should not be used on patients responding to routine therapy. Before using, please read the prescribing information. It's summarized below.

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Tablets of 100 mg.

Important Note: This drug is not a simple analgesic. Do not administer casually. Carefully evaluate patients before starting treatment and keep them under close supervision. Obtain a detailed history, and complete physical and laboratory examination (complete hemogram, urinalysis, etc.) before prescribing and at frequent intervals thereafter. Carefully select patients, avoiding those responsive to routine measures, contraindicated patients or those who cannot be observed frequently. Warn patients not to exceed recommended dosage. Short-term relief of severe symptoms with the smallest possible dosage is the goal of therapy. Dosage should be taken with meals or a full glass of milk. Patients should discontinue the drug and report immediately any sign of: fever, sore throat, oral lesions (symptoms of blood dyscrasia); dyspepsia, epigastric pain, symptoms of anemia, black or tarry stools or other evidence of intestinal ulceration or hemorrhage, skin reactions, significant weight gain or edema. A one-week trial period is adequate. Discontinue in the absence of a favorable response. Restrict treatment periods to one week in patients over sixty.

Indications: Acute gouty arthritis, rheumatoid arthritis, rheumatoid spondylitis.

Contraindications: Children 14 years or less; senile patients; history or symptoms of G.I. inflammation or ulceration including severe, recurrent or persistent dyspepsia; history or presence of drug allergy; blood dyscrasias; renal, hepatic or cardiac dysfunction; hypertension; thyroid disease; systemic edema; stomatitis and salivary gland enlargement due to the drug; polymyalgia rheumatica and temporal arteritis; patients receiving other potent chemotherapeutic agents, or long-term anti-coagulant therapy.

Warnings: Age, weight, dosage, duration of therapy, existence of concomitant diseases, and concurrent potent chemotherapy affect incidence of toxic reactions. Carefully instruct and observe the individual patient, especially the aging (forty years and over) who have increased susceptibility to the toxicity of the drug. Use lowest effective dosage. Weigh initially unpredictable benefits against po-

tential risk of severe, even fatal, reactions. The disease condition itself is unaltered by the drug. Use with caution in first trimester of pregnancy and in nursing mothers. Drug may appear in cord blood and breast milk. Serious, even fatal, blood dyscrasias, including aplastic anemia, may occur suddenly despite regular hemograms, and may become manifest days or weeks after cessation of drug. Any significant change in total white count, relative decrease in granulocytes, appearance of immature forms, or fall in hematocrit should signal immediate cessation of therapy and complete hematologic investigation. Unexplained bleeding involving CNS, adrenals, and G.I. tract has occurred. The drug may potentiate action of insulin, sulfonylurea, and sulfonamide-type agents. Carefully observe patients taking these agents. Nontoxic and toxic goiters and myxedema have been reported (the drug reduces iodine uptake by the thyroid). Blurred vision can be a significant toxic symptom worthy of a complete ophthalmological examination. Swelling of ankles or face in patients under sixty may be prevented by reducing dosage. If edema occurs in patients over sixty, discontinue drug.

Precautions: The following should be accomplished at regular intervals: Careful detailed history for disease being treated and detection of earliest signs of adverse reactions; complete physical examination including check of patient's weight; complete weekly (especially for the aging) or an every two week blood check; pertinent laboratory studies. Caution patients about participating in activity requiring alertness and coordination, as driving a car, etc. Cases of leukemia have been reported in patients with a history of short- and long-term therapy. The majority of these patients were over forty. Remember that arthritic-type pains can be the presenting symptom of leukemia.

Adverse Reactions: This is a potent drug; its misuse can lead to serious results. Review detailed information before beginning therapy. Ulcerative esophagitis, acute and reactivated gastric and duodenal ulcer with perforation and hemorrhage, ulceration and perforation of large bowel, occult G.I. bleeding with anemia,

gastritis, epigastric pain, hematemesis, dyspepsia, nausea, vomiting and diarrhea, abdominal distention, agranulocytosis, aplastic anemia, hemolytic anemia, anemia due to blood loss including occult G.I. bleeding, thrombocytopenia, pancytopenia, leukemia, leukopenia, bone marrow depression, sodium and chloride retention, water retention and edema, plasma dilution, respiratory alkalosis, metabolic acidosis, fatal and nonfatal hepatitis (cholestasis may or may not be prominent), petechiae, purpura without thrombocytopenia, toxic pruritus, erythema nodosum, erythema multiforme, Stevens-Johnson syndrome, Lyell's syndrome (toxic necrotizing epidermolysis), exfoliative dermatitis, serum sickness, hypersensitivity angitis (polyarteritis), anaphylactic shock, urticaria, arthralgia, fever, rashes (all allergic reactions require prompt and permanent withdrawal of the drug), proteinuria, hematuria, oliguria, anuria, renal failure with azotemia, glomerulonephritis, acute tubular necrosis, nephrotic syndrome, bilateral renal cortical necrosis, renal stones, ureteral obstruction with uric acid crystals due to uricosuric action of drug, impaired renal function, cardiac decompensation, hypertension, pericarditis, diffuse interstitial myocarditis with muscle necrosis, perivascular granulomata, aggravation of temporal arteritis in patients with polymyalgia rheumatica, optic neuritis, blurred vision, retinal hemorrhage, toxic amblyopia, retinal detachment, hearing loss, hyperglycemia, thyroid hyperplasia, toxic goiter, association of hyperthyroidism and hypothyroidism (causal relationship not established), agitation, confusional states, lethargy; CNS reactions associated with overdosage, including convulsions, euphoria, psychosis, depression, headaches, hallucinations, giddiness, vertigo, coma, hyperventilation, insomnia; ulcerative stomatitis, salivary gland enlargement. (B)98-146-800-F (10/71)

For complete details, including dosage, please see full prescribing information.

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LA PRUEBA EN LAMINA DE 3 MINUTOS QUE DETECTA EL EMBARAZO



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anti-inflammatory

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the bare facts...

Plain topical steroids alone are not unilaterally recommended if the skin lesion has become infected with fungi or bacteria.

With its four-way action, Vioform-Hydrocortisone provides the kind of comprehensive therapy many common dermatoses* require.

This drug has been evaluated as possibly effective for these indications. See brief prescribing information.

Vioform®-Hydrocortisone (iodochlorhydroxyquin and hydrocortisone)

INDICATIONS

Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, FDA has classified the indications as follows:

"Possibly" effective: Contact or atopic dermatitis; impetiginized eczema; nummular eczema; infantile eczema; endogenous chronic infectious dermatitis; stasis dermatitis; pyoderma; lichenoid eczema and chronic eczematoid otitis externa; acne vulgaris; localized or disseminated neurodermatitis; lichen simplex chronicus; anogenital pruritus (vulvae, scroti, ani); folliculitis; bacterial dermatoses; mycotic dermatoses such as tinea (capitis, cruris, corporis, pedis); moniliasis; intertrigo. Final classification of the less-than-effective indications requires further investigation.

CONTRAINDICATIONS

Hypersensitivity to Vioform-Hydrocortisone, or any of its ingredients or related compounds; lesions of the eye; tuberculosis of the skin; and most viral skin lesions (including herpes simplex, vaccinia, and molluscum contagiosum).

WARNINGS

This product is not for ophthalmic use.

In the presence of systemic infections, appropriate systemic antibiotics should be used.

Use in Pregnancy

Although topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use in pregnant females has not been established. Therefore, they should not be used extensively in pregnant patients in large amounts or for prolonged periods of time.

PRECAUTIONS

May prove irritating to sensitized skin in rare cases. If this occurs, discontinue therapy. May stain.

If used under occlusive dressings or for a prolonged period, watch for signs of pituitary-adrenal axis suppression.

May interfere with thyroid function tests. Wait at least one month after discontinuance of therapy before performing these tests. The ferric chloride test for phenylketonuria (PKU) can yield a false-positive result if Vioform is present in the diaper or urine.

Prolonged use may result in overgrowth of nonsusceptible organisms requiring appropriate therapy.

ADVERSE REACTIONS

Few reports include: Hypersensitivity, local burning, irritation, pruritus. Discontinue if untoward reaction occurs. Rarely, topical corticosteroids may cause striae at site of application when used for long periods in intertriginous areas.

DOSAGE

Apply a thin layer to affected areas 3 or 4 times daily.

HOW SUPPLIED

Cream, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearyl alcohol, spermaceti, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of 5 and 20 Gm. **Ointment**, 3% iodochlorhydroxyquin and 1% hydrocortisone in a petrolatum base; tubes of 5 and 20 Gm. **Lotion**, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearic acid, cetyl alcohol, lanolin, propylene glycol, sorbitan trioleate, polysorbate 60, triethanolamine, methylparaben, propylparaben, and perfume Flora in water; plastic squeeze bottles of 15 ml. **Mild Cream**, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a water-washable base containing stearyl alcohol, spermaceti, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of 1/2 and 1 ounce. **Mild Ointment**, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a petrolatum base; tubes of 1/2 and 1 ounce.

Consult complete product literature before prescribing.

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Vioform® Hydrocortisone (iodochlorhydroxyquin and hydrocortisone)

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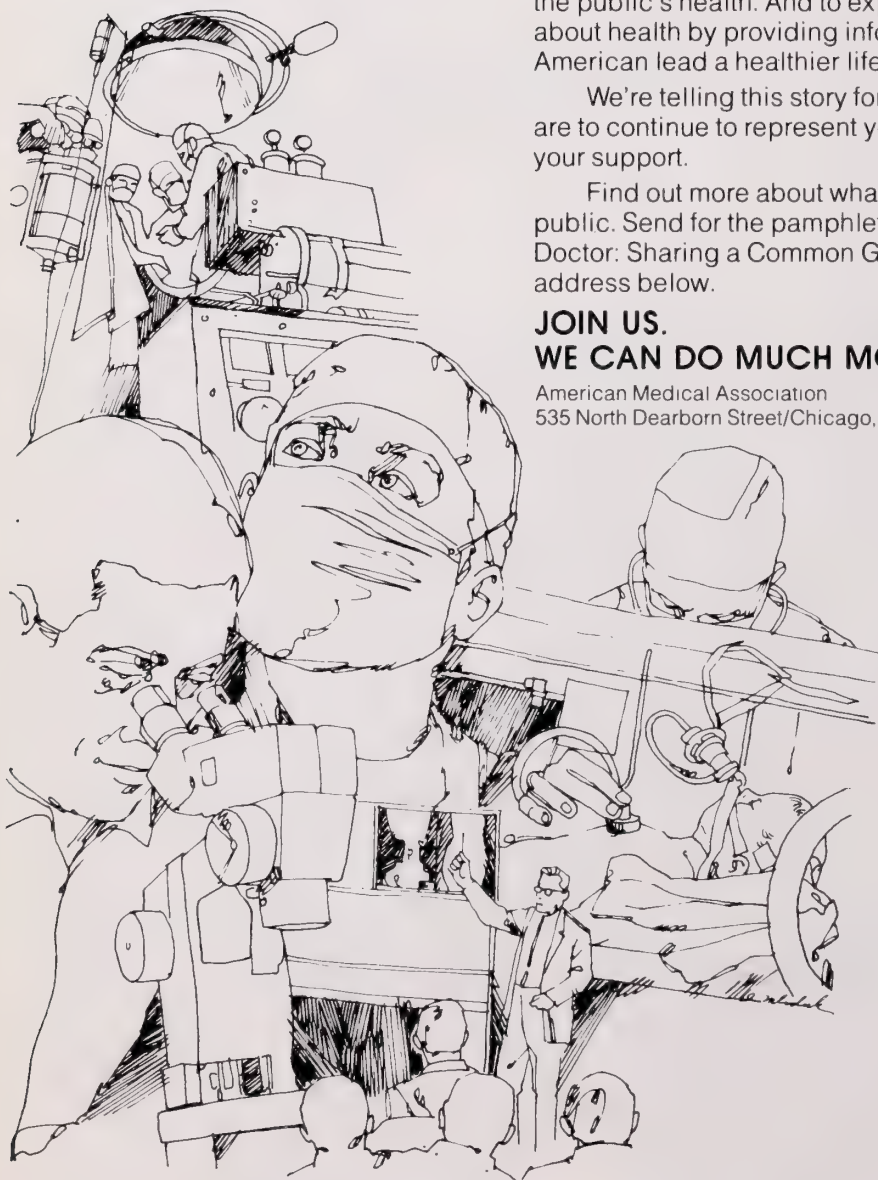
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DOCTORS, DEFENSES AND THE AGE OF INFORMED CONSENT (SECOND PART)

Lou Ashe, JD, LL.M

Doctors as well as lawyers are often at a loss to understand the nature of so-called "privileged communication". Were it not so, we would not have available to us so many reported cases in courts of appeal. Even at that stage of the proceedings, there are various conflicts in the opinions of the courts.

Let's start with a definition. My colleague, Professor Rutter, puts it this way:

"A Privilege is a rule of law which permits a witness to refrain from giving testimony which he otherwise would be compelled to give (or, which allows one of the parties to prevent the witness from testifying) in order to protect a specific relationship or interest."

This rule really reflects a public policy determination which protects the particular relationships or interests involved and considers this to be more important than any testimony which a witness might otherwise be competent to give.

A. Privileged Communications between Physician and Patient

A privilege is something of a personal nature. It can be claimed only by the person or persons whose relationship the law seeks to protect. For example: wife, husband, patient, client, priest and parishioner. As it pertains to the physician-patient relationship, the privilege is not recognized by common law, but has in most states been created by legislation. Its purpose is to encourage full disclosure between patient and physician which is so necessary to the effective treatment of any illness.

A patient, whether or not he is a party to the action, has a privilege to refuse to disclose, and to prevent his physician from disclosing, any information acquired by the physician in confidence while attending the patient.

Although the privilege belongs to the *patient*, if the patient is not present, the doctor is authorized and is ethically obligated to assert the privilege on the patient's behalf in most states. However, if the patient waives the privilege, the doctor may be compelled to testify.

The privilege applies not only to communication between doctor and patient, but to *any information*

obtained by the doctor in the course of examination or treatment which would normally be regarded as confidential. It would also cover results of laboratory tests, x-rays, advice given by the doctor to the patient, as well as opinions resulting from examination.

However, there are certain exceptions, as for example in the following instances:

- a. *a. Personal injury suit by patient (or wrongful death action by his estate).*
- b. *Competency, guardianship and commitment proceedings, affecting the patient.*
- c. *Deceased patient* – The privilege doesn't apply in will contests involving the patient's will.
- d. *Malpractice cases* – The patient cannot prevent his physician from testifying in any case in which the patient has asserted a claim against the doctor for malpractice.
- e. *Illegal purpose:* Also, no privilege exists where the consultation was for an illegal purpose (e.g., to procure an abortion).

The Doctrine of Informed Consent

A. Basic Considerations

There are a number of concepts which have found expression in modern discussions of the doctrine of informed consent. Some courts see it as a problem of the individual right to self-determination vs. the exercise of the therapeutic discretion of physicians and surgeons to withhold information. Others state flatly that the patient's right to make up his own mind regarding what happens to his own body should not be delivered by the courts to the customary local practices of any profession.

The earlier decisions in this area reflected opposing philosophical concepts as to the genesis of liability. According to old classical legal thinking, Professor David Louisell tells us that if in fact consent was "uninformed", that is, if the physician failed to communicate what he should have communicated, and if no voluntary, willing consent was given by the patient, then there was *no consent at all*, and the technique used, the unauthorized procedure involved, amounted

in law to a touching of the person, or a battery. If the philosophy was one of battery, then the plaintiff would be entitled not only to nominal damages, but the more significant factor would be his right to recover punitive damages. If the theory is that the physician has negligently failed to communicate, for whatever reason, then this harsh concept of damages is beyond consideration. Nevertheless, there are those legal scholars who advocate, even today, that we retain the battery concept for those cases where the patient is operated without his consent at all or a procedure performed upon him which he has expressly prohibited. This situation takes on a completely different posture, as may well be realized.

Now that we are in the era of transplantation, more problems are arising, for we are having thrust upon us the potential involvement of the concept of informed consent in these situations. For example, when a still naturally beating heart is removed, how immune is the surgeon from criminal prosecution? It is interesting to note that both Dr. Barnard and Dr. Denton Cooley have stopped performing heart transplants, at least for the time being. Other surgeons seem to be similarly inclined. If we were to indulge further in basics, I would say that wherever serious injury might result, a court is likely to hold that disclosure of the consequences, side effects and the like should be made. I would share with you other of Professor Louisell's admonitions, who tells us:

"Where the procedure in question is electric or insulin shock therapy, both of which involve high incidences of serious injury, the physician is generally held liable for failure to disclose the dangers. Likewise, the patient must be warned where *unorthodox or radical methods of treatment* are to be used or where *potentially dangerous diagnostic or surgical procedures*, such as aortography, are proposed. Where a procedure or other treatment is safe, and the patient is so advised, but it becomes dangerous as the physician proceeds, the patient must be informed, if possible, and given a chance to decide whether he wants to take the risk. A *warning must be given where a potentially lethal drug is prescribed*, especially if it is not generally accepted as necessary or suitable to the patient's disease. The *danger of burns must be disclosed when x-rays or other radiation treatments are given*. Where more than one method of treatment is available, the patient should be informed of the *alternative surgical possibilities* and be given a chance to decide before the operation. Thus, in a case involving prostate surgery

and the cutting of the spermatic cords, the patient should be told that cutting the cords will produce sterility, but that not cutting them increases the possibility of infection which can have very serious results."

When the investigation reveals that the physician actually was unaware of the risks or hazards involved, there is still a different problem. "Obviously, it is impossible to disclose something of which one is unaware," says one writer on the subject. . . "If the risk is not actually known to the physician, it is inappropriate to speak solely of a duty to disclose. *Instead*, a second dimension of the class of risks a doctor should disclose appears — the physician's duty to have known of the risks so he could have discussed them."

In 1957, our California Supreme Court in one of the landmark malpractice decisions (*Salgo v. Leland Stanford, Jr. Board of Trustees*), tried to cover all the possibilities. After noting the obligation of a physician to reveal all the facts necessary for the "patient to form an intelligent consent to the proposed treatment", it continued:

". . . the physician may not minimize the known dangers of a procedure or operation in order to induce his patient's consent. At the same time the physician must place his patient's welfare above all else and this sometimes places him in a position where he must sometimes choose between two alternative courses. One is to explain to the patient every risk attendant upon a surgical procedure or operation, however remote; this may well result in alarming a patient who is already unduly apprehensive and who may as a result refuse to undertake the surgery in which there is in fact minimal risk; it may also result in actually increasing the risks by reason of psychological results of apprehension itself. The other is to recognize that each patient represents a separate problem, that the patient's mental and emotional condition is important and in certain cases may be crucial and that in discussing the element of risk a certain amount of discretion must be employed consistent with the full disclosure of facts necessary to an informed consent."

B. The Modern Scene. The Physician's Affirmative Duty To Reveal.

Observing the modern scene, we note that the courts are willing to recognize the physician's right to the exercise of therapeutic discretion, but the burden remains with him to show *affirmatively* an occasion for his failure to acquaint the patient with the material

risks attendant upon a particular proposed course of treatment.

An Illinois case of February, 1971, resulted in a verdict against the physician who gave the patient an explanation of the proposed angiography, but failed to warn of the dangers of the procedure. After the angiography the 67-year old patient suffered serious residuals. Suit followed against two doctors involved and the hospital. The doctors admitted the procedure was dangerous, but that they withheld the hazards to avoid frightening the patient. There was testimony by an expert that good medical procedure at that time required that the patient be advised of all the possibilities.

A Pennsylvania court in December, 1971, upheld a jury verdict against a physician for failure to disclose fully the risks of a gastroscopic examination. Here, the patient signed a "blanket form consent" authorizing whatever tests her physician deemed necessary. She was told that the gastroscopic examination was a relatively simple procedure and no trouble was anticipated. No information regarding collateral risks were discussed. During the procedure the stomach was perforated. In the lower court a verdict was returned in favor of the physician. The jury had been instructed that the physician's conduct must be measured against the amount of disclosure that would have been made by a reasonable practitioner in the medical community. This instruction in the law was claimed to be erroneous.

The upper court reversed and granted a new trial stating that informed consent requires that a patient be informed of all the material facts from which he can make an intelligent choice. . . *regardless of whether or not he chooses rationally*; that since the patient must bear the expense, pain and suffering of any injury from medical treatment, he has a right to know all the facts which a *reasonable man* would consider material to his decision.

Earlier this year, in a landmark opinion, the District of Columbia Circuit Court recently reaffirmed the physician's duty to reasonably inform an ailing patient of the treatment alternatives available and the material risks incident to them. In this case, a neurosurgeon was held liable for negligent performance of a laminectomy to correct a suspected ruptured disc. The charge was failure of the surgeon to disclose or reveal the risk of paralysis from this surgical procedure. The surgeon had advised the then minor plaintiff's mother that the recommended operation was no more serious "than any other oper-

ation". The hospital liability stemmed from the fact that after the operation the plaintiff was left completely unattended by nursing personnel, and in attempting to void he slipped off the side of the bed, fell to the floor and, among other things, suffered virtually total paralysis from the waist down. At the time of the trial, 11 years later, he was still required to walk with crutches, suffered from urinal incontinence, paralyzed bowels, and was obliged to wear a penile clamp.

Here, as in other cases, the defense contended that disclosing risks to the patient was not good practice because it might deter or dissuade patients from undertaking needed surgery; that the patient might also have adverse psychological reactions, foreclosing a successful operation.

This appellate court first rejected what still appears to be the majority rule, which required expert medical evidence to sustain an alleged failure to obtain informed consent. The court was emphatic in its decision that such a prevailing rule is an "*unwarranted abdication to the medical profession of responsibility and the individual's right to make an informed choice.*" To put it frankly, the court refused to permit the medical profession to determine entirely what the patient should be told; that the individual patient's right to make up his own mind should *not* be delegated by the court to the customary local practice of any profession. Further, the responsibility for the patient's right to self-determination should be a rule which is *imposed by law* for physicians, rather than one which physicians may or may not impose on themselves.

On this basis the patient is not required to produce expert medical testimony of the doctor's negligence in surgery or other treatment or deviation from "standard medical practice"; the patient need only show that the doctor failed to provide information which could have made a difference in the patient's decision.

I would respectfully suggest to my brothers in medicine that the CANTERBURY CASE is must reading. Interestingly, the Court quite rightly recognizes room for a physician's therapeutic discretion in exercising his duty of disclosure. However, it rejects, as I have pointed out, the notion that medical evidence of local professional practice is necessary before a jury may find a doctor negligent in failing to make it.

Even as the print was drying on the decision in the CANTERBURY case, the California Supreme Court put at rest some of the conflicting views in lower appellate courts of the state. The decision announced October 30, 1972 was headlined: "*Doctor Has A Duty To Explain Treatment Choices to Patient*". The surgeon

involved had been treating one Mr. Cobbs for a duodenal ulcer. Surgery followed during which the surgeon severed an artery with resultant serious hemorrhage. After further treatment, Mr. Cobb's spleen was removed and he subsequently developed a gastric ulcer. Speaking to the element of "informed consent" involved, the Court ruled that a doctor *has a legal duty to disclose to his patient the available choices of treatment and the dangers involved in each of them*; that an adult person of sound mind has the right, in the exercise of control over his own body, to determine whether or not to submit to lawful medical treatment.

Mr. Justice Mosk admonished further that for the patient to be able to give an informed consent to treatment there is a duty on the medical doctor to reveal "whatever information is material to the decision"; that the test for determining whether a potential peril must be divulged is its materiality to the patient's decision.

The court added that disclosure of all potential dangers need not be made "if the procedure is simple and the danger remote and commonly appreciated to be remote"; that where the patient is without the mental capacity to reach a rational decision, disclosure is not required.

Disagreeing with the doctor's contention that the duty to disclose is governed by the medical practice in the community, the court found that there is a duty imposed by law for reasonable disclosure which cannot be circumscribed by community medical practice.

How does one write a conclusion to this essentially old, but now revitalized concept — this duty of the doctor to disclose follows logically from the relationship of trust and confidence which must come into play between him and the patient? We who are in "public service" must adjust our thinking so as to accept, in this era of consumer concern, the maturing solicitude of the law for the rights of the individual with whom we must ever deal in scrupulous good faith. This is not to mean that the basic right of the physician to practice his art is, or will be, sacrificed to some zealous over-protection of the patient. The law deals always with reason and what the reasonably prudent and trained physician might be required to do or refrain from doing under a given set of circumstances.

Defensive Medicine: Plan, Panacea or Provocation?

Recently, a well known American lawyer with an

established reputation as a novelist turned to the medical arena for his latest book. Not surprisingly, he called it "MALPRACTICE". One of my well meaning colleagues of the Illinois Bar, thinking to fill in a few of the trying hours while I was temporarily a guest in one of Chicago's famous hospitals (and receiving excellent care), brought me a copy of the book. Inadvertently, I left it on my night stand. The word "malpractice" glared from the shining cover. To compound the situation there alongside lay an envelope with a letter from my dear partner, Mr. Belli. Some four interns and one resident dropped in on "rounds" and I thanked the Good Lord they had a sense of humor. No sooner had the resident examined me and invited comment from the interns, when one of them said: "Let's get out of here before we get sued!"

Let's depart from the fiction for a moment and treat with the realities of the situation. In recent times at gatherings such as this, where lawyers have been permitted to join with their brothers in medicine in free and open discussion — of physicians, patients and inter-professional relationships, I have heard a chorus of voices being raised in response to what a certain segment of your learned profession has characterized as unjustified harassment resulting from multitudinous liability claims. Although it has been variously described, basically it has come to be known as "Defensive Medicine".

Understandably, those of us who have spent trying years preparing for our respective professions and diligently pursuing avenues leading to increased expertise and understanding, may, with considerable justification, feel offended when either our motives, the character of our public service, our devotion to ethical standards or our ability is challenged by a client or patient layman who charges us with carelessness in performance of our professional undertaking.

The lawyer in me insists on a definition of the phrase "defensive medicine", much as my colleagues in medicine ask for and must have a diagnosis before undertaking any definitive treatment. Defensive Medicine, it appears to me, is allegedly that response provoked by the rising statistics of malpractice litigation and to which certain elements of the medical profession react in a variety of ways to express their hostility and indignation. It is a form of *modus operandi* generated and fostered by the basic apprehensiveness of doctors who regard themselves as candidates for a patient's lawsuit. Some of my medical friends have slowly arrived at the feeling, whether justified or not, that getting up in the morning and going to the office to practice medicine is in itself a very real

major hazard. As a layman, I am disturbed by the inherent threat of reprisal involved in this characterization of medical practice. It is often said, "primum no nocere" — (First, no harm to the patient!)

There are learned observers who suggest that part of the problem giving stimulus to malpractice suits is "fragmentation", depersonalization, social and racial inequity, greater emphasis on treatment than prevention of disease, escalating expenses and other manifestations of deteriorating physician-patient relationships. And finally, pure failure to do that which ought to have been done or doing things basically medically contraindicated in good practice.

A number of years ago, Mr. William McPeak, then Vice President of the Ford Foundation, speaking on the layman-patient on the occasion of the dedication of the Stanford University Medical Center, said:

"In medical care he is a layman, dealing with the expert on the expert's ground, and acting alone. He has no platform and is a member of no organized group. . . With the present supply of physicians, he is a buyer in a seller's market. . . One of my premises is that this weakness in the patient's voice, together with correspondingly dominant voice of the doctor, produces dissatisfaction in the patient and can result on occasion in substandard medical care."

Instead of using his time aggressively attacking the pathology presented to him, it is suggested the physician, put on the "defensive" by the ungrateful patient who has brought suit against a fellow doctor, will spend more time analyzing the safe and conservative course of treatment he may offer his own patient.

Regardless of his clinical impressions and ultimate diagnosis, he may order multitudinous laboratory tests, whether medically indicated or not, and exhaust every possible established laboratory aid in every case. To avoid possible charges that he failed to call in a consultant, he will bring one or more into the case. If the patient presents a problem where the prognosis is poor, he may wholly refuse to undertake the case and send the patient packing somewhere else.

If his years of expertise reject the diagnosis of a fracture of the ankle and the clinical impression is a sprain or strain of the joint, in "self defense" he may order a series of x-rays, admit the patient to the hospital, keep him at bed rest and non-ambulatory until both he and two concurring radiologists are satisfied that "there ain't no fracture — no way!" If the patient or the insurance carrier claims "overtreatment" — the answer is simple. "It's either that, or my company may be defending me in a malpractice case!"

Even more than this, is there inherent in the practice of "defensive medicine" a refusal to consider and use highly successful but slightly hazardous medical procedures. (I keep thinking of some of my sexagenarian friends, concerned about their sexual prowess, haunting their doctors insisting on prescriptions for L Dopa.) The justification for all this appears to be that although the cost to the patient is increased, the hazards to the attending physician may be reduced. But is this really the answer? Does it solve the problem or create still another one? Well, before we answer that question, perhaps we should view the patient stripped of emotion. It is my humble opinion, and one which I feel is sustained by much of medical literature, that the patient who receives from his physician positive assurance and a sense of security, a feeling that he has placed his medical problem in safe and expert hands, will have considerably increased chances of recovery. Unquestionably, emotional satisfaction and relief play a substantial part in the healing of organic disease. The therapeutic consolations which flow from a deep respect for one's doctor and faith in his power to heal are very real and often are the most potent of palliatives available to the sick, the dispirited and those in despair. Is maintaining invalidism in deliberately prolonged hospital care the method by which educated men forestall the potential malpractice claimant? If there is clinical evidence of a fracture, swelling, point tenderness, extreme pain, hemorrhaging in the joints, and all this is accompanied by a well recorded history of great trauma to the ankle, do you diagnose without an x-ray? And if one or two views will reveal the fracture, will fear of suits really justify x-rays of both hips, femurs, knees and legs? On the other hand, if a routine chest x-ray reveals some questionable lesion and your expertise is limited in diagnosis of thoracic pathology, will you not agree consultation is required as a matter of ordinary prudence and concern for the patient?

I am of the impression that both of our professions by any ethical and moral standards are irrevocably concerned with the human conduct and more particularly human conduct in response to a myriad of pressures, traumas, and assaults of the modern world. Daily we are called upon to demonstrate our understanding of what makes man act the way he does. The end product of our work is measured by the devotion we maintain toward the ultimate object of our concerns — man, his functions, his mind, his body, his personality and his rightful place in society. We are foresworn to return the injured man to a productive

life commensurate with the injury sustained.

Conclusion

The blessings of your company have been many these last few days full of stimulating programs reflecting great reservoirs of expertise in a variety of medicine's specialties. Believe me that like many of my mature colleagues I am acutely conscious of the fact that thousands of practitioners of your exquisite art are "strangers in the legal paradise"; that the courtroom, lawyers and the intricacies of our evidentiary rules and trial procedures are easily construed as some form of "conspiracy against the caduceus". However, in a nation governed by laws and not men, all stand equal before the law, even those who have attained the highest of scholastic and professional attainments.

Some of my good friends on the defense side of the docket often voice their concern that the image of the lawyer and the doctor is becoming sadly tarnished. One of them at the head of the trial department of a prestigious midwest law firm stated recently:

"... Some are beginning to think of the doctor as a 'super-successful business man'. It is common knowledge today that many doctors are making impressive sums of money, refusing to make house calls, playing golf on Wednesdays, driving expensive cars, owning yachts, lodges and apartment houses. . . This subconsciously makes patients more willing to sue their doctors and the juries more willing to return a verdict. . ."

A spokesman for the American Medical Association testifying before Senator Abraham Rubicoff's Subcommittee on Executive Reorganization stated:

"Medical practice has unavoidably become impersonal. This breakdown in the physician-patient rapport results in part from the growing specialization in medicine. . . Instead of a family physician, the patient may have a whole string of specialists. These are more apt to seem like impersonal business men than like a family friend. . ."

Agreeably, Dr. Vilella Suau's suggestions for the format of our discussion did not require this semantic detour, but I should be derelict if I did not advise you that I know many top flight trial men who wish they never had to try another professional negligence case the rest of their lives. Would that you, our medical brethren, would know the literally hundreds of cases which are

annually rejected in offices around this great country which are determined, at great personal expense in time and money of counsel, to have no merit. Much of this expenditure involves the services of one or more medical specialists who review the marshalled evidence, hospital records, doctor's office records, autopsy records and other documented treatment in order to render an opinion to trial counsel. When a case is finally accepted by a properly trained and competent lawyer, there still remains a tremendous output of time and expense which, at least in the United States, is accomplished on a contingency fee arrangement and with little financial burden upon the injured plaintiff. Only an incompetent, insensitive, poorly motivated lawyer would file a malpractice action for the sake of harassment and the hope of a nuisance settlement.

Would that we could channel the invective, inter-professional distrust and waste energies into constructive channels of communication between both our honored professions. Current moves to minimize the incidents of malpractice action by challenging the contingent fee, developing emotional vendettas against the law and lawyers, attempting to set maximum recovery against any physician regardless of the extent of the negligence in a valid negligence case, denying as a fraud the assertion of reluctance of physicians to give evidence in a malpractice action save on part of the defendant — all this and more, have not served to resolve the problem.

The insurance carrier is no mere shadow in this picture. We are facing some harsh decisions — *law, morals and ethics vs. economics and profits*. We need some first rate chemistry and some hard thinking at levels where the decisions have meaning.

Professions can make claim to ethics and morality only by recognizing the justice of fair compensation from wrong. Modern negligence law actually protects the physician and surgeon from the harsh retaliatory methods and the ravaging methods of the feud, personal battle and assassination by which men sought to avenge the alleged negligence and failures of the early surgeons.

Ultimately, interprofessional bickering and contention must serve to frustrate an already waning public confidence and impugn the integrity of two ancient and honorable professions. As one great philosopher taught us, "It is better to light a candle than to curse the dark!"

CANCER DEL CUELLO DE LA MATRIZ ENTRE LAS MUJERES DE VARONES CON CANCER DEL PENE

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Se han observado incidencias paralelas de carcinoma del cuello uterino y carcinoma del pene en varios grupos poblacionales. Ambos tipos de carcinomas son frecuentes en Puerto Rico (6, 7, 11). En el año 1970 el carcinoma del cuello de la matriz tuvo una tasa de incidencia anual de 45.2 por 100,000 mujeres; el carcinoma del pene tuvo una tasa de 3.5 por 100,000 hombres.

Hay algunos informes que sugieren la posibilidad de un factor común en la patogénesis del cáncer del pene y el cáncer del cuello uterino (1-5, 8, 9, 10, 11).

El objetivo de este estudio fue descubrir la frecuencia en Puerto Rico del carcinoma epidermoide del cuello de la matriz entre las esposas cuyos maridos habían tenido el diagnóstico de carcinoma epidermoide del pene, los intervalos entre los diagnósticos de ambos carcinomas, y comparar los hallazgos con aquellos de otro grupo similar de hombres con otros tipos de tumores malignos.

La situación de la circuncisión se consideró similar en ambos grupos de varones (casos y controles) ya que esta operación no es practicada rutinariamente entre los niños recién nacidos en Puerto Rico; es practicada principalmente entre los recién nacidos de familias de la práctica privada o bien en aquellos niños cuya fimosis es incompatible con una función urinaria normal.

Material y Métodos

El Registro Central del Cáncer de Puerto Rico tiene la responsabilidad de analizar y llevar a cabo el seguimiento de los casos de cáncer diagnosticados por los médicos en todos los hospitales, clínicas, y oficinas privadas de toda la Isla. El Registro opera mediante Legislación que obliga el informe de los casos de cáncer. Además, esta Institución mantiene una búsqueda sistemática para los casos que no se informan, llevando a cabo una búsqueda en todos los Registros de los Patólogos, de los Departamentos de Admisión y de los Departamentos de Records Médicos de los Hospitales.

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De los archivos del Registro Central se revisaron 1064 casos de carcinoma epidermoide del pene histológicamente comprobados (Grupo de estudio) y un número igual de casos en varones con carcinoma de la boca, faringe, esófago, y estómago todos diagnosticados de enero de 1950 a junio de 1972. El segundo grupo (Grupo control) fue pareado con el primero por año de diagnóstico y edad, seleccionados por orden de llegada a los archivos. El cáncer de la boca, de la faringe, el esófago y del estómago ocurren más frecuentemente también en niveles socio-económicos bajos, como también ocurre con los casos de carcinoma del cuello uterino y del pene. Este hecho elimina algún sesgo en la comparación de los dos grupos.

La revisión de los expedientes incluyó el nombre, la edad, la ocupación, la residencia, la fecha de diagnóstico, la situación marital, el nombre de la esposa y su diagnóstico de cáncer, así como la fecha y la etapa en que se diagnosticaron.

Los nombres de las esposas que no aparecieron en los expedientes del Registro Central de Cáncer fueron buscados en los expedientes originales de los hospitales, en los certificados de defunción, y por comunicaciones con sus familias, a través de diferentes agencias de la comunidad, incluyendo el Departamento de la Policía.

Los nombres de las esposas, tanto para los casos como para los controles fueron revisados contra el índice del Registro Central del Cáncer, para investigar si habían sido informados como casos de cáncer. Especial cuidado se tuvo para correlacionar no solamente el nombre completo de la esposa, sino que también la edad, la residencia, y el nombre del esposo en el record correspondiente de ella. En casos de duda, se establecieron comunicaciones con las familias.

Hallazgos

El porcentaje mayor de carcinoma del pene ocurrió en el grupo de edad de 65-69 años (Tabla I). El riesgo de desarrollar la enfermedad aumenta constantemente con la edad.

Aunque la ocupación habitual (Tabla II) no es adecuadamente informada por las personas retiradas, existe, sin embargo, un porcentaje más bajo de casos de carcinomas del pene entre el grupo profesional (2.1 por ciento) que entre el grupo de obreros (15.5 por ciento) de bajos salarios.

El Distrito Noreste de la Isla (Tabla III) es el área de nivel económico más alto y tiene la incidencia más baja de cáncer del pene. Si esta tasa hubiera sido ajustada por edad todavía sería menor, ya que la población

TABLA I: DISTRIBUCION POR EDAD

Grupos	No.	Casos Por Ciento	Prom. Anual Tasa * Incidencia	No.	Controles Por Ciento
< 20	1	0.1	----	1	0.1
20 - 24	4	0.4	0.2	6	0.6
25 - 29	20	1.9	1.4	16	1.5
30 - 34	29	2.7	2.4	34	3.2
35 - 39	53	5.0	4.1	47	4.4
40 - 44	80	7.5	6.8	79	7.4
45 - 49	88	8.3	7.8	93	8.7
50 - 54	102	9.6	11.4	99	9.3
55 - 59	104	9.8	13.7	109	10.3
60 - 64	121	11.4	18.8	112	10.5
65 - 69	145	13.6	26.3	158	14.9
70 - 74	95	8.9	24.5	88	8.3
75 - 79	78	7.3	31.9	77	7.2
80 - 84	69	6.5	62.7	70	6.6
85 - +	65	6.1	64.2	64	6.0
Desconocido	10	0.9	----	10	0.9
Total	1064	100.0	4.1	1063 **	100.0

* - Tasas incidencia por 100,000 habitantes.

** - Un caso joven que no se ha podido parear.

TABLA II: OCUPACION

	No.	Casos Por Ciento	No.	Controles Por Ciento
Profesionales	22	2.1	46	4.3
Empleados Oficina	6	0.6	10	0.9
Trabajadores diestros	42	3.9	141	13.3
Obreros agrícolas	78	7.3	311	29.3
Otros obreros	87	8.2	245	23.0
No informado	829	77.9	310	29.2
Total	1064	100.0	1063	100.0

TABLA III: SITIO DE RESIDENCIA

D istritos	No.	Casos Por Ciento	Prom. Anual Tasa Incidencia	No.	Controles Por Ciento
Norte	169	15.9	5.0	140	13.2
Oeste	146	13.7	4.5	151	14.2
Sur	237	22.3	4.2	269	25.3
Este	177	16.6	4.4	162	15.2
Noreste	312	29.3	3.6	334	31.4
Desconocido	23	2.2	—	7	0.7
Total	1064	100.0	4.2	1063	100.0

TABLA IV: ZONA DE RESIDENCIA

	Casos		Controles	
	No.	Por Ciento	No.	Por Ciento
Rural	557	52.3	584	54.9
Urbana	373	35.1	440	41.4
Suburbana	73	6.9	25	2.4
No informado	61	5.7	14	1.3
Total -	1064	100.0	1063	100.0

TABLA V: ESTADO CIVIL

	Casos		Controles	
	No.	Por Ciento	No.	Por Ciento
Casado	852	80.0	1021	96.0
Soltero	74	7.0	27	2.5
Desconocido	138	13.0	15	1.4
Total -	1064	100.0	1063	100.0

TABLA VI: LOCALIZACION DEL CANCER EN LOS MARIDOS

I. C. D.	Localización	Casos		Controles	
		No.	Por Ciento	No.	Por Ciento
179.0	Pene (Epid.)	1064	100.0	0	0
140 - 144	Boca			280	26.4
145 - 148	Faringe			146	13.7
150.0	Esófago			234	22.0
151.0	Estómago			403	37.9
Total		1064	100.0	1063	100.0

de esta Región es también más vieja. Por el contrario, los Distritos Norte y Oeste tienen las tasas más altas; ellos son también las áreas más pobres de Puerto Rico.

Una correlación similar (Tabla IV) de la incidencia de cáncer del pene con el nivel socio-económico se encuentra en la distribución de los casos por zona de residencia. Solamente 35.1 por ciento de los casos ocurrieron en población urbana, y esta constituye 47 por ciento del total de la población. El ingreso de los grupos urbanos es casi el doble que el de los grupos rurales. Las facilidades sanitarias son, por definición, mejores en las zonas urbanas.

La Tabla número V muestra la distribución de los casos y los controles por su estado civil. Es interesante observar en esta Tabla el porcentaje de hombres con car-

cinoma del pene que aparentemente nunca se casaron. Sospechamos la existencia de algún problema físico y/o psicológico relacionado con la esfera sexual entre este grupo de varones solteros.

En la siguiente Tabla (Tabla VI) se observa la distribución de las localizaciones primarias del cáncer entre los maridos del grupo de control. El porcentaje mayor correspondió a carcinoma del estómago.

En general, (Tabla VII) el grupo de las esposas de los hombres con carcinoma del pene desarrollaron más tumores malignos (32) de lo esperado (15). La frecuencia de carcinoma epidermoide del cuello de la matriz entre las esposas de los varones con carcinoma de pene fue diez veces más alto que entre las esposas del grupo de control y que el número esperado de casos de acuerdo

TABLA VII: LOCALIZACION DEL CANCER EN LAS ESPOSAS

I. C. D.	Localización	Casos Observados	Casos Esperados *	Controles
171.0	Cuello uterino	10	1.5	0
170.0	Seno	3	1.2	2
176.1	Vagina	0	0.0	1
175.0	Ovario	1	0.3	0
140.0 - 159.0	Boca, faringe & sistema digestivo	10	6.2	0
190.0 - 191.0	Piel	5	4.5	4
192.0 - 205.0	Otras localizaciones	3	1.4	0
No informado		1032	1048.9	1056
Total		1064	1064	1063 **

* - De acuerdo al grupo con tasa incidencia más alta.

** - Un caso de cáncer de pene no se pudo aparear debido a la edad.

TABLA VIII: INTERVALO ENTRE EL DIAGNOSTICO DE CANCER DE PENE Y EL DIAGNOSTICO DE CANCER DE CUELLO UTERINO

	Ca. cuello uterino después de Ca. pene	Ca. cuello uterino antes de Ca. pene
6 - 11 meses	1	0
12 - 23 meses	0	2 *
2 - 4 años	2	1 **
5 - 10 años	2	0
10 +	1	1
Total	6	4

* - Etapa avanzada al diagnóstico.

** - Metástasis remota al diagnóstico.

a la tasa de incidencia más alta de los grupos poblacionales en Puerto Rico.

La ocurrencia de 10 casos de cáncer de cervix entre 852 mujeres casadas con hombres con cáncer del pene, en contraste con ningún caso entre 1,021 mujeres casadas con varones con otros cánceres sugiere que no se debe al azar.

Con la excepción de cuatro parejas, (Tabla VIII) el carcinoma del pene fue diagnosticado de 11 meses a 10 años antes que el correspondiente carcinoma del cuello de la matriz en sus mujeres. Sin embargo, en dos de las cuatro excepciones el carcinoma del pene fue diagnosticado en un estadio más avanzado que los correspondientes casos del cáncer del cuello de la

matriz. Esto parece indicar que el carcinoma del pene de estos dos casos se desarrolló también más temprano que el carcinoma del cuello de la matriz en sus correspondientes esposas.

Estos hallazgos nos llevan a sospechar que los carcinomas epidermoides del cuello de la matriz y del pene tienen un factor etiológico común, el cual parece operar más tempranamente en el grupo masculino.

Como consecuencia práctica en el Registro Central del Cáncer, todo caso de cáncer de pene se le busca la esposa y a ésta se le da una cita para hacerle citología de cervix con el objeto de descubrir tempranamente el cáncer del cervix en este grupo de alto riesgo.

Resumen

Se revisaron 1064 casos de carcinoma epidermoide del pene histológicamente confirmados en Puerto Rico de 1950 a 1972. Se seleccionó otro grupo igual de hombres con cáncer de la boca, faringe, estómago y esófago, y se parearon con los primeros por edad y año de diagnóstico. En ambos grupos se buscaron las esposas para saber si habían sido registradas con algún neoplasma maligno, particularmente del cuello de la matriz.

Resalta del estudio el hallazgo de 10 casos de carcinoma del cuello uterino entre las esposas de los casos de cáncer de pene en comparación con ninguno entre las esposas de los controles. La mayoría de los carcinomas del cuello de la matriz fueron diagnosticado más tarde y en etapa más temprana que los carcinomas del pene. Siendo pues alto el riesgo de desarrollar ese cáncer toda mujer de un caso de cáncer de pene debe estudiarse y controlarse cuidadosamente tratando de descubrirle el carcinoma en etapa temprana.

Summary

A group of 1064 cases of epidermoid carcinoma of the penis diagnosed in Puerto Rico from 1950 to 1972 were matched by age and date of diagnosis with a group of men with malignant neoplasms of the buccal cavity, pharynx, esophagus, and stomach. The wives of the two groups were searched in order to see the frequency of carcinoma of the cervix uteri among them, and the sequence and intervals between the two diagnoses. The wives of the penile carcinoma group developed 10 cases of epidermoid carcinomas of the cervix uteri in contrast with none among the control

wives. Eight out of ten carcinomas of the cervix uteri were diagnosed later and in earlier stage than the penile carcinomas. A practical application of this Study is a careful clinical study and close follow-up of wives of men with the diagnosis of cancer of the penis.

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PREVALENCE OF HEPATITIS-ASSOCIATED ANTIGEN (HAA) IN COLLAGEN DISORDERS

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The cause of the collagen-vascular disorders is not yet known. Immunologic responses to viral agents may be important in the pathogenesis in view of the following: recent reports which implicate hepatitis-associated antigen (HAA)-anti-HAA complexes as the cause of arthritis (1), polyarteritis (2), and glomerulonephritis (3); chronic active hepatic disease, in which HAA may be found in up to 25 percent of patients (4), has been said to be related to systemic lupus erythematosus (SLE) (5); and virus-like structures have been found in the tissues of patients with SLE and other collagen disorders (6). The reported prevalence of HAA in collagen disorders is variable and is confined exclusively to polyarteritis (2) and SLE (7, 8).

This paper reports a study of the prevalence of HAA in the sera of patients with various collagen disorders.

Material and Methods

HAA was determined, in the sera of 41 patients with various collagen disorders, by the counterimmunoelectrophoresis method (9). After informed consent was given by the patient, a blood sample was obtained and an interview was conducted. Specific inquiry was made as to previous or current history of hepatitis, contact with hepatitis patients, other liver disorders, jaundice, drug addiction, blood transfusions and injections, leukemia, blood dyscrasia, leprosy, and chronic renal disease requiring hemodialysis. One patient who had an undifferentiated vasculitis was eliminated from the study because of a recent history of hepatitis; HAA was present in her serum. The serum samples were processed by a technician who was not aware of the patient's identity, diagnosis, or history.

Results

The prevalence of HAA in our patients is shown in the Table. Both of the patients with a positive result

for HAA were women. One had SLE and was 45 years old; the other had scleroderma and was 60 years old. Apart from their collagen disorder, their clinical histories were negative and their liver function tests normal. Unfortunately both patients refused to undergo liver biopsy. Of the 38 patients without HAA, 9 had received 1 or 2 units of blood several years prior to the study, and 4 had been in contact with a jaundiced person at some time during their lifetime. None gave a history of overt hepatitis or other significant correlates.

Discussion

The discovery of HAA and the development of various methods for its detection made available a suitable indicator for the presence of a virus in humans. The search for a possible viral role in the pathogenesis of the collagen-vascular disorders has now been extended to include HAA.

Immunologic responses to the hepatitis virus were first implicated in the pathogenesis of rheumatic disorders by Alpert and co-workers in 1970 (1). They found a significant depression of total serum comple-

PREVALENCE OF HAA IN 40 PATIENTS WITH COLLAGEN DISORDERS

Disorder	No. Tested	No. Positive
SLE	22	1
Dermatomyositis and polymyositis	6	0
Scleroderma	4	1
Undifferentiated vasculitis	3	0
Sjögren's syndrome	1	0
Necrotizing vasculitis	1	0
Takayasu's arteritis	1	0
Chronic discoid lupus	2	0
Total	40	2

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ment and one or more of its components (C1q, C4, or C3) in the presence of circulating HAA in seven patients with acute viral hepatitis who manifested arthralgia and arthritis of the distal joints and proximal interphalangeal joints, fever, and urticaria. Subsequently, Gocke and co-workers (2) found HAA in 4 of 11 patients with clinically typical, biopsy-proved polyarteritis nodosa. Three of these four were shown to have circulating HAA-immunoglobulin complexes in their sera; one was found to have deposits of HAA, IgM, and β_{1C} in the blood vessel walls. This report probably represented the first recognition, in man, of a systemic vasculitis mediated by an immunologic reaction to a virus or virus-like particle. Likewise, granular deposits of HAA, IgG, and β_{1C} were found by Combes and co-workers (3) in the glomeruli of a man with persisting hepatitis, HAA, and membranous glomerulonephritis. Since no HAA was found in control glomeruli from four other patients (two with lupus nephritis and immune deposits in their glomeruli; one heroin addict with recent HAA-negative hepatitis and nephrotic syndrome; and one HAA-positive renal transplant recipient dying of fulminant hepatitis), the authors concluded that the antigen was responsible for the initiation of the glomerular process.

In spite of these sporadic associations (highly suggestive of viral pathogenesis), a broad relationship between collagen disorders and HAA remains to be established. Prince and Trepo (10) found that the presence of HAA-anti-HAA complexes did not correlate well in the presence or absence of chronic active hepatic disease (CAHD) or polyarteritis nodosa. They concluded that, although the pathogenesis of both probably involves immune mechanisms, these are not mediated by HAA-anti-HAA antibody complexes. Although HAA may be present in up to 25 percent of patients with CAHD, and 15 percent of patients with CAHD may have a positive LE cell test, a much lower percentage of patients with both CAHD and HAA have had a positive LE cell test (4, 11). Almost all reported patients with CAHD and a positive LE cell test have not had a positive assay for HAA (11). Gocke and Kavey (12), using immunodiffusion, detected no HAA in the sera of 22 patients with connective tissue diseases. By a similar method, no HAA was found by Mathews and MacKay (13) in the sera of 18 patients with autoimmune disorders other than chronic hepatitis. Furthermore, Panush and associates (14) examined, by counterimmunoelectrophoresis, the sera of 201 patients with adult and juvenile rheumatoid arthritis, SLE, scleroderma, or polymyositis and the synovial fluid of 43

patients with rheumatoid arthritis and found negative results for both HAA and anti-HAA.

In contrast, Alarcón-Segovia and Fishbein (7), using a complement-fixation method, detected HAA in the sera of 25 percent of their 75 SLE patients. These same sera were negative for HAA by immunodiffusion. A positive result also was obtained by Ziegenfuss *et al* (8) in the sera of two girls with SLE and lupus nephritis tested by counterimmunoelectrophoresis. Many factors, including the method used for detection of HAA and the presence of anticomplementary factors in the sera, probably limit the frequency of detection of HAA in the sera of collagen disease patients.

One of our 22 patients with SLE had a positive HAA assay. Moreover, one patient with scleroderma was positive for HAA. We have not found any reports of the presence of HAA, apparently unrelated to liver disease, in patients with scleroderma. The practical implications of our findings are hard to establish because of the size of our sample and the absence of other immunologic data to support a pathogenetic or other role for HAA in these patients. Certainly, the possibility that certain collagen disorders may be caused by immune responses to HAA or the hepatitis virus is an attractive one.

However, the fact that virus-like structures have been found in cells of 52 SLE and 4 systemic sclerosis patients (6), that HAA has been found with variable frequency in the sera of patients with SLE and now of one patient with scleroderma, and that a probable pathogenetic relationship between HAA and some cases of polyarteritis has been established should encourage investigators to conduct a more detailed and specific search for the nature of the relationship between HAA and the collagen disorders. The use of the more sensitive radioimmunoassay for HAA detection and of immunologic tissue studies will certainly be of help in this quest.

Summary

Immunologic responses to viral agents appear to be important in the pathogenesis of some cases of collagen-vascular disorders. Hepatitis-associated antigen (HAA) has been implicated in the pathogenesis of polyarteritis nodosa, arthritis, and glomerulonephritis and has been found to be associated less strongly with systemic lupus erythematosus (SLE). The presence of HAA in the sera of 2 of 40 patients with collagen-vascular disorders (one with scleroderma and one with SLE) in the apparent absence of liver disease is reported. No previous association has been reported between HAA and scleroderma.

Resumen

Las respuestas inmunológicas a los agentes virales parecen ser importantes en la patogénesis de algunos casos de enfermedades del colágeno. Se ha implicado el HAA en la patogénesis de poliarteritis nodosa, artritis, y glomerulonefritis, y también en asociación menos directa con lupo eritematoso sistémico (SLE). Se informa la presencia de HAA en el suero de 2 de 40 pacientes con enfermedades del colágeno (uno con escleroderma y uno con SLE) que presumiblemente no tienen enfermedad hepática. La asociación de HAA y escleroderma no ha sido informada previamente.

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LA PRESERVACION EXPERIMENTAL Y CLINICA DE RIÑON PARA TRASPLANTE

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El trasplante de riñón como tratamiento de la insuficiencia renal terminal se está utilizando cada día más en los centros especializados. Para intentar vencer la disparidad entre el número de recipientes y posibles donantes, ha tomado auge la investigación en la preservación de órganos. Éxito excelente en preservación renal ha sido logrado por Belzer (1, 2), Collins (3), y otros (4, 5, 6). Con las técnicas de preservación se ha podido utilizar más efectivamente el número limitado de órganos de cadáver. Igualmente, ha permitido tiempo para mejor tipificación entre donante y recipiente, mejor preparación del recipiente, y mejores órganos trasplantables.

La mayoría de los sistemas actuales están basados en perfusión con plasma homólogo, cuyas crio-proteínas y lipoproteínas han sido ya precipitadas (1). Este plasma es recirculado a través de un sistema que incluye un oxigenador, un enfriador y una bomba pulsátil, cuya complejidad mecánica es variable.

Como el uso de estos sistemas es complicado, difícil y laborioso, hemos diseñado una serie de experimentos para intentar simplificar la metodología y la técnica lo más posible. Todas las facetas envueltas en la preservación renal fueron evaluadas y cuestionamos la necesidad de los distintos componentes de cada máquina. Estos experimentos culminaron en el diseño de un sistema de preservación renal relativamente sencillo, transportable, y de construcción, manejo, preparación y utilización fácil.

Comparación de Métodos para Preservación Renal

Hemos querido investigar si es necesaria la presencia de plasma homólogo y de circulación constante, ya que Collins (3), utilizando un perfusado de composición similar al líquido intracelular, logró resultados acepta-

bles. Para probar esta hipótesis, usamos tres grupos de riñones caninos. Un grupo fue preservado utilizando perfusión inicial con la solución de Collins (C4), seguido de preservación en salina helada. Un segundo grupo, utilizó perfusión pulsátil con la técnica de Belzer, y un tercer grupo utilizó una combinación de ambos: 6 horas de Collins, seguidos de 18 horas de perfusión pulsátil. Tras 24 horas de preservación, se reimplantó el riñón en la fosa iliaca izquierda del donador, seguido de nefrectomía contralateral.

Los resultados se demuestran en la Tabla I. Encontramos que tan solo 50 por ciento de los riñones preservados con hipotermia y solución de Collins podían sostener función suficiente para sobrevivir post-trasplante. En contraste, 88 por ciento de los riñones preservados por 24 horas por medio de perfusión pulsátil tuvieron función normal. Aun hipotermia en combinación con perfusión resultó en una sobrevida reducida. Concluimos que la perfusión pulsátil es mejor que la perfusión inicial con Collins, aun cuando sea seguida por perfusión. Dos estudios recientes (7, 8) sin embargo, han demostrado éxito clínico con la solución de Collins. Explicamos esto a base de que, en la situación clínica, el mejor manejo pre y post-trasplante y el uso de hemodiálisis post-operatoria, pueden resultar en una mejor sobrevida.

Comparación de Métodos en la Preservación del Riñón Isquémico

Para mejor simular la situación clínica, decidimos utilizar un modelo experimental que resultara en daño isquémico como el que se observa en la situación clínica. Utilizamos el mismo modelo de preservación por 24 horas seguido de implantación y nefrectomía contralateral. A diferencia del experimento anterior, ocluimos el pedículo vascular del riñón por 20 minutos, antes de removerlo y preservarlo.

Con este período de isquemia normotérmica (warm ischemia) se hizo más evidente la diferencia entre los distintos métodos de preservación (Tabla I). Al hacer una nefrectomía contralateral inmediata, encontramos que la sobrevida con hipotermia y solución de Collins

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TABLA I: SOBREVIDA CON DIFERENTES METODOS DE PRESERVACION

Método de Preservación	Sin Isquemia Nefrectomía Inm.		20 Minutos Isquemia Normotérmica Nefrectomía Inm. Nefrectomía Tardía			
Hipotermia (24 hrs.)	6/13	(47 por ciento)	0/4	(0 por ciento)	0/5	(0 por ciento)
Hipotermia (6 hrs.) + Perfusión (18 hrs.)	3/6	(50 por ciento)	0/6	(0 por ciento)	7/8	(85 por ciento)
Perfusión (24 hrs.)	16/18	(88 por ciento)	3/10	(30 por ciento)	9/9	(100 por ciento)

TABLA II: SOBREVIDA CON DROGAS EN PRESENCIA DE ISQUEMIA *

Ruta de Administración	Metilprednisolona		Clorpromazina		Fenoxibenzamina	
Endovenoso-pre Isquemia	4/4	(100 por ciento)	4/4	(100 por ciento)	2/4	(50 por ciento)
Arteria Renal-post Isq.	4/4	(100 por ciento)	3/4	(75 por ciento)	2/4	(50 por ciento)
Lavado Lactato de Ringer's	4/4	(100 por ciento)	2/4	(50 por ciento)	---	
Perfusión con Plasma	4/4	(100 por ciento)	3/4	(75 por ciento)	2/4	(50 por ciento)

* Nefrectomía Contralateral Inmediata
Sobrevida sin drogas = 30 por ciento (Tabla I)

fue de 0 por ciento y con perfusión pulsátil fue de 30 por ciento. Si permitimos que el riñón contralateral quede en su sitio para luego hacer una nefrectomía contralateral tardía, encontramos que la supervivencia usando hipotermia y Collins es todavía de 0 por ciento y que estos riñones jamás recobraron su función. Sin embargo una combinación de hipotermia con perfusión, o perfusión sola permite una supervivencia mucho más adecuada. Concluimos de estos estudios que un sistema basado en perfusión pulsátil es mejor que un sistema con solución de Collins e hipotermia, en la preservación de órganos con daño isquémico (9).

Diseño de un Sistema Sencillo de Preservación (Mox-100)

En vista de estos estudios decidimos diseñar nuestro propio aparato de perfusión renal. Esta decisión fue

basada en la complejidad y dificultad de esterilización, preparación y manejo de otros aparatos existentes (Belzer: L.I. 400, Woods: Mox 300). El objetivo era el de obtener un aparato compacto, sencillo en su operación, esterilización y preparación, y además convenientemente transportable (10).

Alterando la configuración geométrica y el tamaño del sistema circulatorio, hemos diseñado una "caseta" que incorpora la cámara de órganos, la reserva venosa, metro, oxigenador, reserva arterial, bomba pulsátil, y el enfriador (figura 1). Esta caseta plástica viene estéril, pero puede ser re-esterilizable en gas. El sistema opera por gravedad y la circulación la provee en bomba de pistón. La caseta es intercambiable entre una unidad portátil y la consola principal del hospital. Funciona con corriente eléctrica pero puede funcionar también con batería.

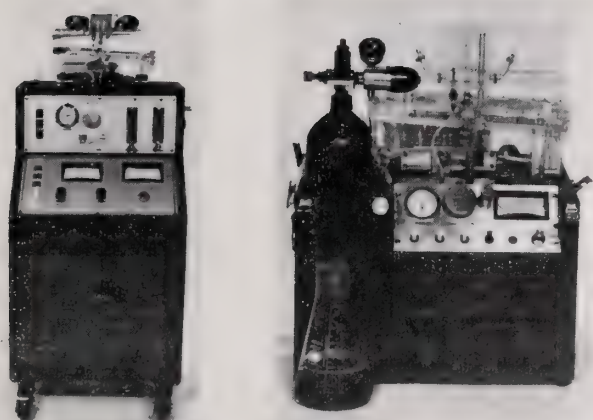


Fig. 1: Izquierda: Muestra la caseta como se describe en el texto, descansando sobre la consola que controla la bomba, la infusión de gases, y la unidad de Freon. Derecha: Modificación transportable de la consola, la cual funciona con batería, y mezcla de gases. Sus dimensiones permiten acomodo en el asiento de un automóvil o avión pequeño.

Comparación del Sistema Mox-100 con Otros Sistemas

Para probar que la eficiencia no se había perdido al disminuir el tamaño y redistribuir los componentes, se comparó este sistema con los sistemas existentes de Belzer y Woods. Utilizamos el mismo modelo experimental de perfusión por 24 horas seguido de implantación y nefrectomía contralateral. Un grupo de 9 animales fue utilizado en cada máquina. Aunque la función renal fue mejor en el sistema Mox-100 durante la primera semana post-trasplante, al finalizar un período de dos semanas, la función renal y la sobrevida de los tres grupos fueron estadísticamente idénticos (4). Concluimos de esto que el sistema Mox-100 era tan eficaz como los sistemas ya previamente probados.

Simplificación del Problema de la Isquemia

La isquemia que se observa durante la agonía del donante cadáver es un problema que afecta la calidad final del órgano trasplantado. Para intentar alterar los efectos de la isquemia y así simplificar la preservación, se diseñó un experimento utilizando el modelo de oclusión vascular produciendo isquemia, seguido de preservación por 24 horas, y luego implantación y nefrectomía contralateral. El efecto protector de varias drogas se comparó. Metilprednisolona, clorpromacina, y fenoxibenzamina, fueron adminis-

tradas por cuatro rutas diferentes antes y después del insulto isquémico. Estas rutas y los resultados se resumen en la Tabla II. Irrespectivo de la ruta, la metilprednisolona resultó en protección completa del órgano isquémico, resultando en una sobrevida de 100 por ciento (11). En contraste, la fenoxibenzamina, droga de predilección en otras instituciones (2, 12), no fue tan efectiva. Además de mejorar la sobrevida, la metilprednisolona resultó en un retorno a función normal el segundo día post-trasplante, en contraste con la clorpromacina que tardó 6 días en retornar a lo normal, y la fenoxibenzamina que tardó 14 días en retornar a función normal (11). En conclusión, hemos comprobado que la utilización de agentes protectores celulares mejoran la sobrevida y la función de riñones con daño isquémico. Como resultado de estas observaciones, hemos adoptado la utilización de la metilprednisolona en todos los riñones de donante cadáver (13).

La Simplificación del Perfusado

La preparación del plasma de perfusión es laborioso y requiere equipo especial. Se obtiene sangre homóloga, se separa el plasma, se congela, y luego se descongela y se filtra para remover las lipoproteínas que se precipitan en frío. Se filtra, se esteriliza, se le añaden electrolitos y manitol, se determina su concentración, se añade un indicador y luego se utiliza para perfusión. Idealmente, debíamos tener un perfusado que se pueda obtener comercialmente, y que no requiera esterilización ni preparación alguna. Investigaciones por algunos grupos en Europa han demostrado que albúmina es adecuada aun en la situación clínica (12).

Para duplicar estos resultados y simplificar esta área, intentamos utilizar preparaciones comerciales de albúmina existentes en los Estados Unidos. Utilizamos el modelo experimental sin isquemia, perfundiendo con plasma o con albúmina por 24 horas, seguido de implantación y nefrectomía contralateral. Obtuvimos los siguientes resultados: 9 de 10 animales perfundidos con plasma sobreviven con su trasplante, y 7 de 7 sobreviven con albúmina. Sin embargo el retorno de función a lo normal es de 3 días o menos con el plasma y de 4 a 10 días con la albúmina. Al utilizar un modelo con isquemia por 20 minutos, seguido de preservación con albúmina o con plasma, y luego implantación y nefrectomía contralateral, obtenemos los siguientes resultados: 8 de 8 animales preservados con plasma sobreviven, mientras que solo 2 de 5 animales preservados con albúmina so-

TABLA III
EXPERIENCIA CLINICA (MOX-100)
Abril, 1971 — Abril, 1972

	Universidad de Minnesota		Centros Múltiples	
<i>Núm. Riñones Perfundidos</i>	40		139	
<i>Núm. Trasplantados</i>	36	(90 por ciento)	117	(84 por ciento)
Compartidos	7	(19.4 por ciento)	19	(16.2 por ciento)
<i>Núm. No Usado</i>	4	(10 por ciento)	22	(16 por ciento)
Incompatibles	1		18	
Error Técnico	1		2	
Falla de Preservación	2		2	
<i>Función</i>	35	(97 por ciento)	96	(91 por ciento)
Inmediatamente	29	(82 por ciento)	63	(60 por ciento)
Tardía	6		33	
Ninguna	1		9	
<i>Sin Función</i>	1		9	
Rechazo			7	
Técnica	1		1	
Falla de Preservación			1	

breviven. La función renal retorna a lo normal antes del quinto día en los animales de plasma, y de 12 a 14 días en los animales con albúmina. Se concluye que albúmina puede ser un sustituto adecuado para el plasma si no hay un insulto isquémico envuelto. Sin embargo al haber daño isquémico, la perfusión con plasma sigue siendo ideal, y mucho mejor que la perfusión con albúmina. No obstante, el uso de un perfusado sencillo como la albúmina, merece más investigación.

Experiencia Clínica

Resumimos nuestra experiencia clínica con el sistema Mox-100 en la Tabla III. En la Universidad de Minnesota, 90 por ciento de los riñones perfundidos con nuestro sistema fueron trasplantados y 82 por ciento funcionaron inmediatamente. Insulto isquémico estaba presente en 30 por ciento a 40 por ciento de nuestros casos, pero fue solo en situaciones con isquemia prolongada (hasta 90 minutos) los que resultaron en el 15 por ciento de daño funcional (necrosis tubular aguda). Factores técnicos quirúrgicos o técnicos en la preparación del plasma resultaron en la no-utilización de tres riñones.

El sistema Mox-100 ha sido utilizado en otros centros

en Estados Unidos y esta experiencia también se presenta en la Tabla III. Función inmediata tan solo la obtuvieron en 60 por ciento, y esto se puede explicar a base del uso de hipotermia sencilla para transportación, además de la perfusión, mientras que en nuestro servicio utilizamos la perfusión por máquina desde el comienzo. A pesar de estos episodios de disfunción temprana, la inmensa mayoría retorna a una función completamente normal a las dos o cuatro semanas después del trasplante.

Resumen

1. La logística del trasplante renal, sobre todo en cadáveres, requiere un método de preservación y transportación de órganos que sea confiable.

2. Al presente, el modo óptimo de preservar riñones debe incluir hipotermia, perfusión pulsátil con plasma homólogo crioprecipitado, y oxigenación.

3. Se ha diseñado un sistema que simplifica grandemente la operación técnica de la perfusión, y a la vez es suficientemente pequeño y compacto para ser portátil.

4. La preservación de órganos puede ser simplificada y a la vez ser confiable.

5. El sistema Mox-100 se ha probado en la situación

experimental, comparándolo con otros métodos de preservación, al igual que con otros sistemas y aparatos ya probados, y compara favorablemente, aun en la presencia de daño isquémico. Experiencia clínica es excelente.

6. Un oxigenador de membrana pequeño puede ser utilizado efectivamente y todavía retener poder de reserva.

7. Metil-Prednisolona y Clorpromacina en dosis adecuadas y por rutas específicas pueden proteger el riñón con daño isquémico.

8. El plasma crioprecipitado debería ser simplificado, pero las soluciones de albúmina comercial disponibles son al presente un sustituto inferior.

Reconocimiento

Agradecemos al Sr. Tom Burton y la Compañía Waters, de Rochester, Minnesota, su ayuda valiosa en el desarrollo de este sistema. Igualmente agradecemos a los Sres. Howard Cummings y Les Olson, su ayuda técnica.

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(Prepared by The Office of the General Counsel of the American Medical Association)

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Therefore, in purchasing the practice of a retiring or deceased physician, the purchasing physician may not acquire the medical records of the patients without the express written consent and direction of the patient. Of course, the patient may not be solicited for this consent by either the purchasing or the selling physician. The proper procedure would be for the retiring physician or the family of the deceased physician to notify the patient of the fact of the doctor's death or retirement and advise the patient that his or her medical records will be transferred to whichever physician the patient wishes to consult, but that the patient must advise the physician in writing. In the normal course of this procedure, the purchasing physician will probably get the largest portion of the patients. He should receive for his use only the records of those patients who have elected to be treated by him.

What about the records of those patients who do not authorize the transfer of their medical records? If they cannot be transferred, can they be destroyed? Actually,

destruction may be a great disservice to both the patient and the physician (or the physician's estate). These records may be important in defending a malpractice claim against the physician or against his estate. It may, in fact, be the only defense available. Therefore, for the protection of the physician and his estate, the records should be retained for at least the period of the Statute of Limitations and remember that this statutory period does not apply against minor patients until after they reach the age of majority, usually 21 years age. There are also occasionally other exceptions and circumstances which extend the period of the Statute of Limitations, so due consideration should be given to these factors before any records are destroyed. Also, these records may contain information that is vital to the later treatment of the patient; or perhaps the information in the records would be helpful in assisting the patient to qualify for an insurance policy, or a new job, or in the patient's claim for injuries resulting from an accident. It would be wasteful to destroy such potentially valuable records. It would be nice to think that the records would remain in existence as long as the patient lived, but, of course, this must be balanced against the limitations involved in retaining the records. Modern computers may eventually solve the problems of space and cost in the storage and retrieval of records. In the meantime, some local medical societies have undertaken to store the records of their deceased members.

We would suggest that the records of those patients who do not authorize the transfer of their records to the purchasing physician or another physician, may be entrusted to the purchasing physician for safekeeping. It is possible that a patient, sometime after the sale is conducted, may want his records transferred to another physician, and this patient would probably go back to the office of his original physician seeking those records.

(To be continued)

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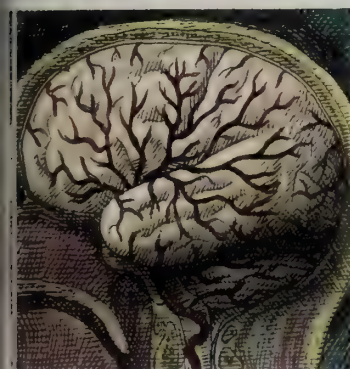
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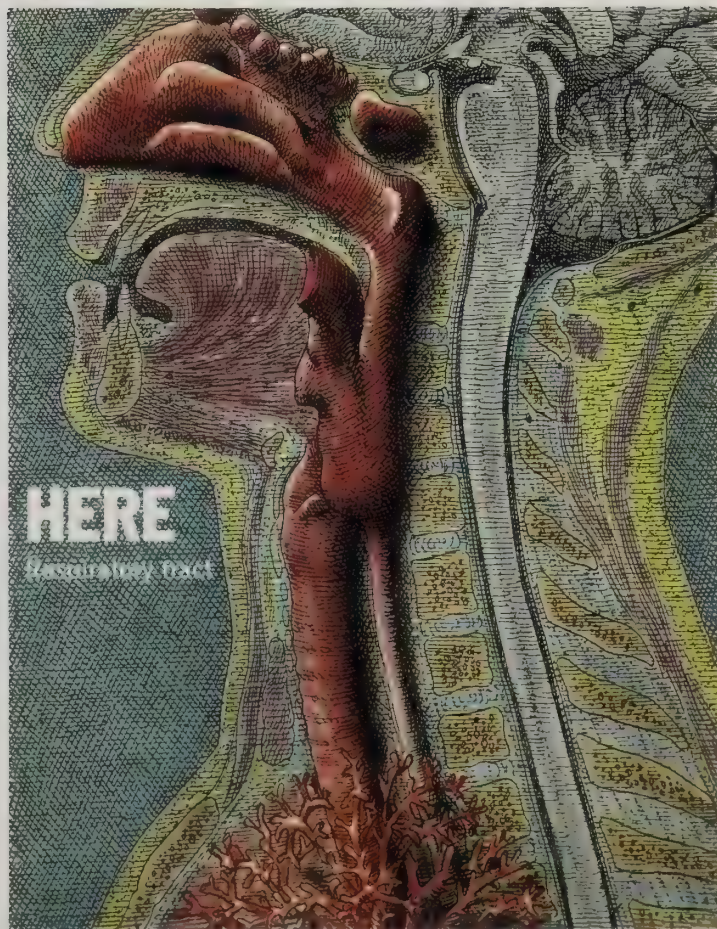
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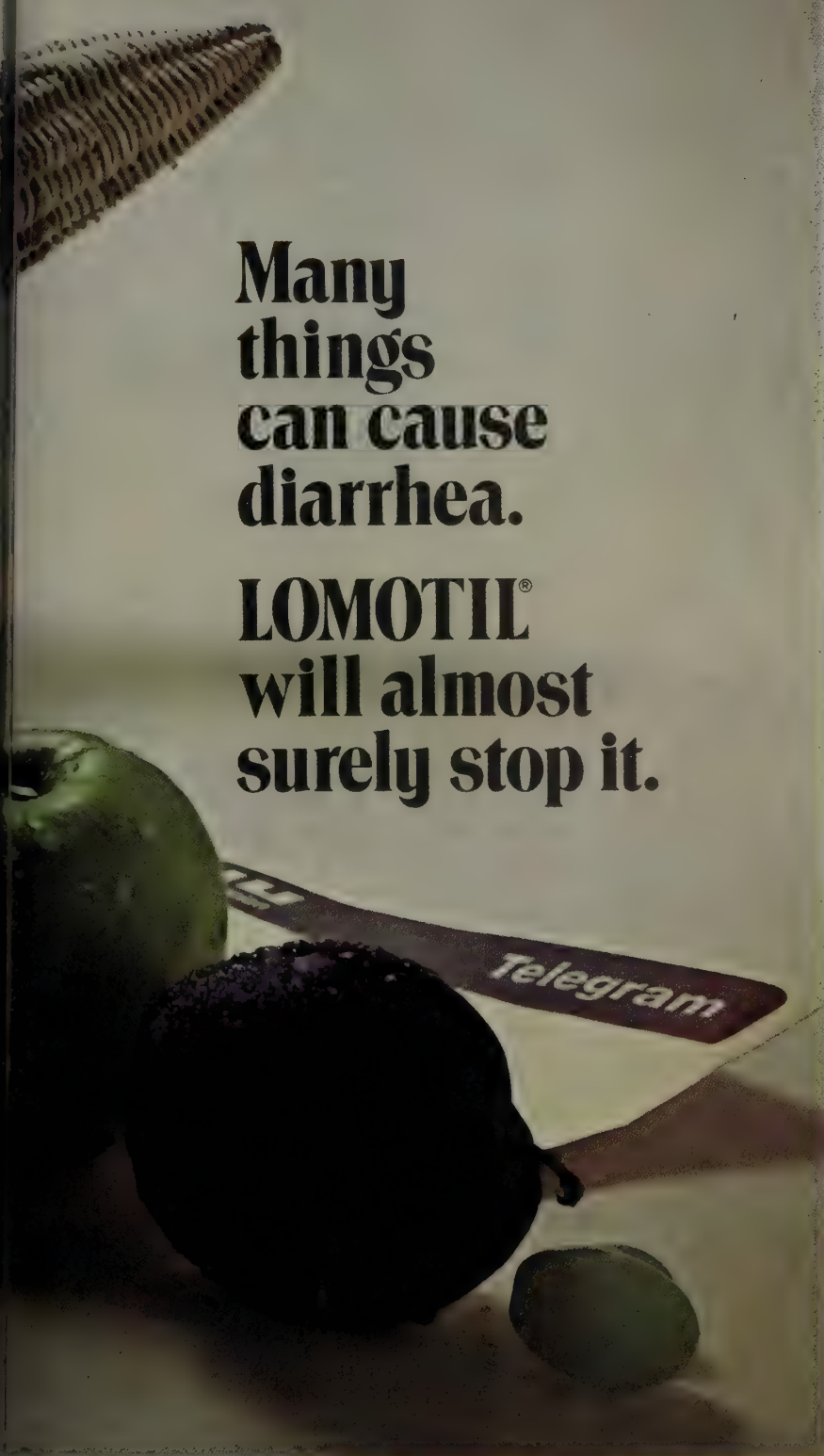
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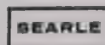
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Contraindications: Hypersensitivity to any component; concurrent MAO inhibitor therapy; severe hypertension; bronchial asthma; coronary artery disease; stenosing peptic ulcer; pyloroduodenal or bladder neck obstruction. Children under 6.

Warnings: Caution patients about activities requiring alertness (e.g., operating vehicles or machinery). Warn patients of possible additive effects with alcohol and other CNS depressants.

Usage in Pregnancy: In pregnancy, nursing mothers and women who might bear children, weigh potential benefits against hazards. Inhibition of lactation may occur.

Effect on PBI Determination and I¹³¹ Uptake: Isopropamide iodide may alter PBI test results and will suppress I¹³¹ uptake. Substitute thyroid tests unaffected by exogenous iodides.

Precautions: Use cautiously in persons with cardiovascular disease, glaucoma, prostatic hypertrophy, hyperthyroidism.

Adverse Reactions: Drowsiness, excessive dryness of nose, throat or mouth; nervousness; or insomnia. Also, nausea, vomiting, epigastric distress, diarrhea, rash, dizziness, weakness, chest tightness, angina pain, abdominal pain, irritability, palpitation, headache, incoordination, tremor, dysuria, difficulty in urination, thrombocytopenia, leukopenia, convulsions, hypertension, hypotension, anorexia, constipation, visual disturbances, iodine toxicity (acne, parotitis).

Supplied: Bottles of 50 capsules.

SK&F Smith Kline & French Laboratories

OPINIONES

LA ASOCIACION MEDICA DE VILLATURBIA

La Asociación Médica de Villaturbia elegía su presidente cada seis meses. Había un presidente actuante, un presidente entrante, un presidente saliente y un presidente corriente (el presidente corriente corría, pero no llegaba).

La asociación estaba afiliada a la *Homokan Medical Association*, y, cuando los oficiales de allá estornudaban, a los de acá les daba catarro. Lo de elegir los presidentes cada seis meses, al igual que todo lo que se hacía en la asociación de Villaturbia, era una copia exacta de lo que se hacía en Homokan. Nadie se detenía a pensar si lo del presidente nuevo cada seis meses era bueno o malo. Bastaba que en Homokan se hiciera.

Según el reglamento, había que colocar un retrato al óleo de cada presidente saliente, de dos pies de ancho por tres de largo, en algún sitio prominente del edificio de la asociación. Ya estaban llenas de retratos todas las paredes de los pasillos y los salones principales, desde el techo hasta el piso, y todo el mundo estaba preocupado pensando qué iban a hacer con los retratos de los nuevos presidentes, cuando se cubriera la única pared que quedaba.

En las asambleas médicas de Villaturbia, los trabajos se presentaban en inglés, salvo alguna que otra excepción. La excepción solía ser algún profesor eminente de España, o de la América hispana, que pedía permiso para hablar en español. Este profesor tenía que sentarse horas y horas a oír a los médicos

de Villaturbia gaguear unos con otros en inglés, y, cuando se dormía, lo llamaban para que presentara su conferencia en la olvidada lengua de Cervantes.

La Escuela de Medicina de Villaturbia enseñaba en inglés. Al igual que la asociación médica, no hacía nada por prestigiar el idioma vernáculo. Cada día que pasaba era mayor la brecha de incomprensión entre estas dos instituciones y el pueblo a que debían servir.

Los médicos de Villaturbia eran buenos. Algunos de ellos eran de los mejores del mundo; pero les faltaba algo. Se habían especializado exageradamente. Sabían mucho de poco, y no tenían la comprensión universal que se requiere para entender las ansiedades y angustias de un pueblo.

La Asociación Médica de Villaturbia estaba intensamente preocupada, porque los servicios médicos eran cada vez más costosos, y el pueblo ya no podía resistir la carga. Se hablaba de organizar un Seguro de Salud Universal, y se le pedía a la asociación que se uniera al pueblo en el empeño de hallar un modo de rendir servicios médicos de alta calidad a pobres y ricos por igual. ¿Cómo hacerlo? Había un deseo genuino de ayudar; pero las dudas eran muchas, porque la cooperación exigía nuevos enfoques y actitudes, y había que buscar la inspiración en Villaturbia, y no en Homokan. Mientras tanto, el tiempo pasaba con rapidez, y el pueblo esperaba, con una mezcla de ansiedad y esperanza.

José Rodríguez Pastor, M. D.



Julian Katz, M.D.
Assistant Professor of
Medicine and Director,
Clinical Research Laboratory,
Section of Gastroenterology,
Medical College of Pennsylvania

Gastrin: an updated look at an important hormone

Early in this century Edkins showed that the intravenous injection of an extract of antral mucosa would stimulate gastric acid secretion. He gave the name gastrin to this proposed hormone. After Komarov substantiated the presence of such a hormone, Gregory and fellow workers isolated, characterized, and synthesized the polypeptide. Gastrin not only has an important influence on acid secretion, but also plays a major role in other gastrointestinal functions.

Structure

Antral gastrin contains 17 amino acids. It is remarkable that a 4 amino acid segment, the carboxyl terminal portion, can reproduce all the activities of which the whole molecule is capable.

Gastrin and feedback mechanism of acid secretion

Gastrin is produced primarily by the mucosal cells in the gastric antrum, the distal non-acid secreting portion of the stomach. The hormone stimulates the parietal cells in the fundus and body of the stomach to produce acid, and a negative feedback mechanism is initiated. Acid bathing the antrum acts directly on the gastrin-producing cell to inhibit release of the hormone.

Gastrin and the lower esophageal sphincter

Contraction of the gastroesophageal sphincter is stimulated by

gastrin. The sphincter muscle is more sensitive to the effects of gastrin than adjacent esophageal muscle. The efficacy of antacid therapy in reflux esophagitis may be due, in part, to the release of antral gastrin. Antacids neutralize gastric acid and raise the pH in the antrum. The gastrin which is then released increases the strength of the sphincter, which acts as a barrier against reflux.

Some other actions of gastrin

Beyond gastrin's prime role as a stimulator of gastric acid production, gastrin also acts on other parts of the G.I. tract. On the stomach, to stimulate (albeit weakly) pepsin production and increase gastric antral motility. On the pancreas, by stimulating enzyme secretion. On the liver, by increasing the flow of bile. On the intestine, by inhibiting absorption of water and electrolytes, and—possibly—increasing motility. And, on the ileocecal sphincter, by relaxing it (contrary to its action on the gastroesophageal sphincter), and perhaps contributing to the gastro-colic reflex.

Excessive gastrin production

It would be expected that if the stomach could not produce acid, gastrin release would continue unabated. Indeed such is the case in pernicious anemia, where there is achlorhydria, and circulating gastrin levels are very high. Alka-

linization of the antrum, vagal stimulation, and mechanical distension of the antrum all provoke gastrin release.

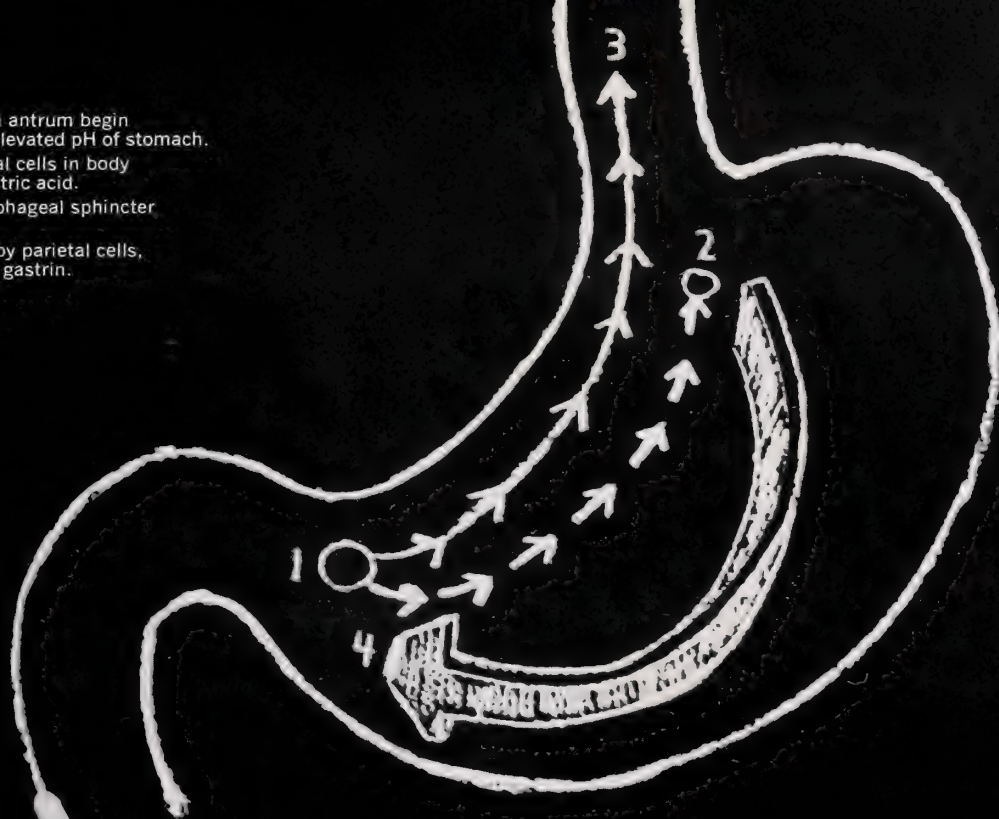
In the Zollinger-Ellison syndrome the radioimmunoassay of gastrin may be the best diagnostic technique. The islet-cell tumor produces large amounts of gastrin, leading to gastric hypersecretion and often intractable ulcer disease. Another situation in which gastrin levels may be high, is when the antrum is retained after gastric resection. Here the antrum is removed from the inhibitory effects of acid, and hypersecretion of gastrin occurs.

Some therapeutic implications

Obviously surgical removal of the antrum will lower gastric secretion as therapy for peptic ulcer disease. But other ways of antagonizing gastrin are being investigated. Some substances have a close structural similarity to the gastrin molecule. For example, cholecystokinin, the intestinal hormone, and caerulein, a material extracted from the skin of amphibians, contain in their structure a sequence of amino acids identical to the active terminal portion of gastrin. These substances are competitive inhibitors of gastric secretion. They combine with the receptor site for acid secretion, cause little stimulation of the receptor, and thus occlude the site.

Keys

1. Gastrin-producing cells in antrum begin secreting in response to elevated pH of stomach.
2. Gastrin stimulates parietal cells in body and fundus to secrete gastric acid.
3. Contraction of gastroesophageal sphincter facilitated by gastrin.
4. Resulting HCl, produced by parietal cells, inhibits further release of gastrin.



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NOTICIAS

HEW NEWS:

Proposed Medicare regulations to revise payment procedures for institutional providers of health services were announced today by HEW Secretary Caspar W. Weinberger.

The proposed regulations would terminate the special payment procedure that provided funds to hospitals in advance of regular billing. They implement the Administration's decision to end this procedure, as announced on January 29, in the President's 1974 budget, and will result in the recovery of outstanding advances of approximately \$300 million in fiscal year 1973.

Secretary Weinberger pointed out that there was a need for the special financing procedure at the beginning of the Medicare program in 1966 because of concern that substantial numbers of institutional health care providers would decline to participate in the program due to the possibility of long delays in routine reimbursements. The procedure provided working capital advances in advance of billings that were calculated to place the providers of Medicare services in the same position as if they were reimbursed concurrent with the time they were giving the services.

The claims reimbursement process is now well established and provides for payments periodically on a regular basis, not less often than monthly, following the submission of bills. Since the original concern over large backlogs has been eliminated, the so-called current financing procedure — which involves substantial loss of interest earnings by the Medicare Trust Fund — is no longer appropriate, Mr. Weinberger said.

If delays in payment occur in unusual situations, an accelerated payment may be made to a provider of services where the provider has experienced financial difficulties due to a delay by a Medicare intermediary in making payments or, in exceptional situations, where the provider of services has experienced a temporary delay in preparing and submitting bills beyond its normal billing cycle.

Interested parties have 30 days from April 2, 1973, the date of publication of the proposed regulations in the Federal Register to submit comments.

AMA NEWS FEATURES:

CHICAGO — The tragedy of an amputated limb has been relieved somewhat by artificial arms and legs as close to natural as space-age technology can make them. But the scientific

horizon may hold an ultimate — and incredible — solution: Growing a new limb.

"I believe that by affecting the proper hormone balance and using electricity, we can produce regeneration," Dr. Robert O. Becker said several years ago in outlining planned experiments. And since then he has achieved some limb regeneration in rats and frogs, animals which do not normally regenerate missing parts (as does, for example, the salamander).

Dr. Becker, associate chief of staff for research at the Veterans Administration Hospital, Syracuse, New York, recently described experiments with four groups of rats. All had their right forelegs amputated. Group 1 rats were left alone to heal naturally, but Group 2 animals had low-current generating devices implanted in their stumps while Group 3 rats got high-current devices. Group 4 animals received devices which generated what the researchers considered the "right" amount of current. The results:

Group 1 rats had normal healing over of the wound. Group 2 animals had more-than-normal bone growth while Group 3 rats had bone destruction.

As for Group 4:

"It was found that, in a high percentage of cases, (there was) regrowth of an organized, multi-tissue portion of the missing extremity," Dr. Becker said. "Tissues regenerated were: bone, cartilage, bone marrow, muscle, nerve and blood vessels. While a complete extremity was not formed in any case, the amount and organizational pattern of the unit formed far exceeds any growth naturally seen or previously obtained by any technique."

The regeneration is caused by electrical simulation of cellular activity. But the electricity must be applied in precisely the right amount. In the rat experiment, the right amount was 3 to 6 nanoamperes, a nanoampere being one-billionth of an ampere. (By comparison, a car battery may use half a dozen amperes).

The electricity causes cells to "dedifferentiate" — to become blastocytes, which are embryo cells not yet embarked on a particular cellular role. Then these cells "redifferentiate" into the missing structure, such as the rat foreleg. Hopefully, sometime in the future, they will be induced to become new hands, arms or legs for human amputees.

Mammals, specifically humans, likely have always had the ability to regenerate but lost the means to utilize it during evolution, Dr. Becker said.

Instrucciones para los Autores

El Boletín acepta para su publicación artículos relativos a medicina y cirugía y las ciencias afines. Igualmente acepta artículos especiales y correspondencia que pudiera ser de interés general para la profesión médica.

El artículo, si se aceptara, será con la condición de que se publicará únicamente en esta revista.

Para facilitar la labor de revisión de la Junta Editora y la del impresor, se requiere de los autores que sigan las siguientes instrucciones:

Manuscrito: El manuscrito completo, incluyendo las leyendas y referencias deberán estar escritos a maquina a doble espacio y por un solo lado de cada página, en duplicado y con amplio margen. En página separada deberá incluirse lo siguiente: título, nombre del autor (es) y su grado (ej: MD, FACP), ciudad donde se hizo el trabajo, el hospital o institución académica, patrocinadores del estudio, y si un artículo ha sido leído en alguna reunión o congreso, así debe hacerse constar como una nota al calce.

El manuscrito debe comenzar con una breve introducción en la cual se especifique el propósito del mismo. Las secciones principales (como por ejemplo: materiales y métodos) deben identificarse como un encabezamiento al centro y en letras mayúsculas.

Artículos referentes a resultados de estudios clínicos o investigaciones de laboratorio deben organizarse bajo los siguientes encabezamientos: Introducción, Materiales y Métodos, Resultados, Discusión, Resumen (en español e inglés), Reconocimiento y Referencias.

Artículos referentes a estudios de casos aislados deben organizarse en la siguiente forma: Introducción, Materiales y Métodos si es aplicable, Observaciones del Caso, Discusión, Resumen (en español e inglés), Reconocimientos y Referencias.

Nomenclatura: Deben usarse los nombres genéricos de los medicamentos. Podrán usarse también los nombres comerciales, entre paréntesis, si así se desea. Se usará con preferencia el sistema métrico de pesos y medidas.

Tablas: Las tablas deben aparecer en hojas separadas. Estas deben incluir el título y el número de la tabla (romano). Los símbolos de unidades deben limitarse al encabezamiento de las columnas. Se deben omitir líneas verticales y horizontales en la tabla.

Figuras: Las fotografías y microfotografías se someterán como copias en papel de lustre, sin montar. En el reverso de la figura debe aparecer el número de la figura (arábigo) y el autor y debe indicarse la parte superior.

Referencias: Las referencias deben ser numeradas sucesivamente de acuerdo con su aparición en el texto. Los números deben aparecer en paréntesis al nivel de la línea u oración. Al final de cada artículo las referencias deben aparecer en el orden numérico en que se citan en el texto. Estas deben seguir el estilo o patrón del "Index Medicus", el cual se describe a continuación:

Para artículos de Revista

Apellido (s), e iniciales del nombre del autor (es), nombre de la revista, volumen, primera página y año.

Koppisch E: Bol Asoc Med P Rico 46: 505, 1954.

Para citación de Libros

Apellido (s), e iniciales del autor (es), título, edición, casa editora, ciudad, año y página.

Wintrobe MM: Clinical Hematology, 3rd Ed Lea and Febiger, Philadelphia 1952 p 67.

Más de tres autores añadir: et al.

Deben usarse solamente las abreviaturas indicadas en el "Cumulative Index Medicus" que publica la Asociación Médica Americana.

Como guía de referencia para preparar su artículo puede usar la publicación Advice to Authors que publica la Scientific Publications Division, American Medical Association, 535 N Dearborn Street, Chicago, Illinois, 60610.

Instructions to Authors

The Boletín will accept for publication contributions relating to the various areas of medicine, surgery and allied medical sciences. Special articles and correspondence on subjects of general interest to physicians will also be accepted. All material is accepted with the understanding that it is to be published solely in this journal.

In order to facilitate review of the article by the Editorial Board and the work of the printer, the authors must conform with the following instructions:

Manuscripts: The entire manuscript, including legends and references should be typewritten double spaced in duplicate with ample margins. A separate title page should include the following: title, authors and their degrees (e. g. MD, FACP), city where the work was done, hospital or academic institutions,

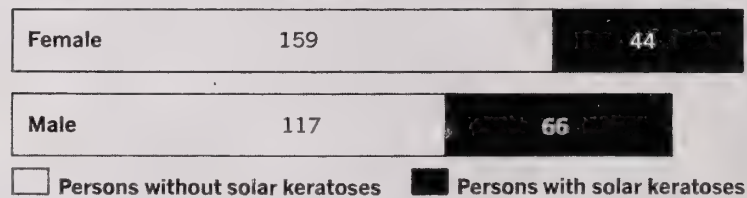
What it means to live and work in Tipton County, Tennessee

**Persons who are white and
over 40 have one chance in four
of having solar keratoses...
which may be premalignant**

An epidemiologic study* conducted in Tipton County, Tennessee, revealed that 28.5% of white persons over 40 had solar keratoses; most had multiple lesions. Cluster sampling projected an estimated prevalence of 32.5% for white males and 19.5% for white females.

Though this is an unusually high percentage of affected persons, these lesions can occur in any white population, wherever people work or play out of doors.

**Prevalence of solar keratoses in white persons
over 40 in Tipton County, Tennessee**



*Data on file, Hoffmann-La Roche Inc., Nutley, New Jersey.



Solar, actinic, senile keratoses

Called by many names, the typical lesion is flat or slightly elevated, brownish or reddish in color, papular, dry, adherent, rough, sharply defined; usually multiple lesions, chiefly on exposed portions of the skin.

Sequence/selectivity of response

Erythema in areas of lesions may begin after several days of therapy; height of reaction (only in affected areas)* usually occurs within two weeks, declining after discontinuation of therapy. Since this response is so predictable, lesions that do not respond should be biopsied to rule out the presence of a frank neoplasm.

Cosmetic results

Cosmetic results are highly favorable. Incidence of scarring is low—important with multiple facial lesions. Efudex should be applied with care near the eyes, nose and mouth.

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Contraindications: Patients with known hypersensitivity to any of its components.

Warnings: If occlusive dressing used, may increase inflammatory reactions in adjacent normal skin. Avoid prolonged exposure to ultraviolet rays. Safe use in pregnancy not established.

Precautions: If applied with fingers, wash hands immediately. Apply with care near eyes, nose and mouth. Lesions failing to respond or recurring should be biopsied.

Adverse Reactions: Local—pain, pruritus, hyperpigmentation and burning at application site most frequent; also dermatitis, scarring, soreness and tenderness. Also reported—insomnia, stomatitis, suppuration, scaling, swelling, irritability, medicinal taste, photosensitivity, lacrimation, leukocytosis, thrombocytopenia, toxic granulation and eosinophilia.

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acknowledgment of financial sponsors, and if the paper has been presented at a meeting the place and date should be given.

The manuscript should start with a brief introductory paragraph or paragraphs which should state its purpose. The main sections (for example, Materials and Methods) should be identified by center headings in capital letters.

Articles reporting the results of clinical studies or laboratory investigation should be organized under the following headings: Introduction, Material and Methods, Results if indicated, Discussion, Summary in English and Spanish, Acknowledgments if any, and References.

Nomenclature: Generic names of drugs should be used; trade names may also be given in parenthesis, if desired. Metric units of measurements should be used preferentially.

Tables: These should be typed on separate sheets with the title and table number (Roman) centered. Symbol for units should be confined to the column headings. Vertical and horizontal lines should be omitted.

Figures: Photographs and photomicrographs should be submitted as glossy prints, unmounted. They should be labeled in the back with the name of the authors and figure number (Arabic) and the top should be indicated. Legends to the figures should

be typed on a separate sheet.

References: These should be numbered serially as they appear in the text. The number should be enclosed in parenthesis on the line of writing and not as superscript numbers. At the end of the article references should be listed in the numerical order in which they are first cited in the text. This list should conform to the Style of the Index Medicus and should be punctuated as in the following examples.

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Koppisch E: Bol Asoc Med P Rico 46: 505, 1954.

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Wintrobe MM: Clinical Hematology, 3rd Ed Lea and Febiger, Philadelphia 1952 p 67.

More than three authors add: et al.

Abbreviations will conform to those used in the Cumulative Index Medicus, published by the American Medical Association.

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tated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

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Before deciding to make Valium (diazepam) part of your treatment plan, check on whether or not the patient is presently taking drugs and, if so, what his response has been. Along with the medical and social history, this information can help you determine initial dosage, the possibility of side effects and the ultimate prospects of success or failure.

While Valium can be a most helpful adjunct to your counseling, it should be prescribed only as long as excessive psychic tension persists and should be discontinued when you decide it has accomplished its therapeutic task. In general, when dosage guidelines are followed, Valium is well tolerated (see Dosage). For convenience it is available in 2-mg, 5-mg and 10-mg tablets.

Drowsiness, fatigue and ataxia have been the most commonly reported side effects.

Until response is determined, patients receiving Valium should be cautioned against engaging in hazardous occupations requiring complete mental alertness, such as driving or operating machinery.



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Nutley, N.J. 07110

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their pre-disposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

Dosage: Individualize for maximum beneficial effect.

Adults: Tension, anxiety and psychoneurotic states, 2 to 10 mg b.i.d. to q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed; adjunctively in skeletal muscle spasm, 2 to 10 mg t.i.d. or q.i.d.; adjunctively in convulsive disorders, 2 to 10 mg b.i.d. to q.i.d. *Geriatric or debilitated patients:* 2 to 2½ mg, 1 or 2 times daily initially, increasing as needed and tolerated. (See Precautions.) **Children:** 1 to 2½ mg t.i.d. or q.i.d. initially, increasing as needed and tolerated (not for use under 6 months).

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Indications: Acute gouty arthritis, rheumatoid arthritis, rheumatoid spondylitis.

Contraindications: Children 14 years or less; senile patients; history or symptoms of G.I. inflammation or ulceration including severe, recurrent or persistent dyspepsia; history or presence of drug allergy; blood dyscrasias; renal, hepatic or cardiac dysfunction; hypertension; thyroid disease; systemic edema; stomatitis and salivary gland enlargement due to the drug; polymyalgia rheumatica and temporal arteritis; patients receiving other potent chemotherapeutic agents, or long-term anticoagulant therapy.

Warnings: Age, weight, dosage, duration of therapy, existence of concomitant diseases, and concurrent potent chemotherapy affect incidence of toxic reactions. Carefully instruct and observe the individual patient, especially the aging (forty years and over) who have increased susceptibility to the toxicity of the drug. Use lowest effective dosage. Weigh initially unpredictable benefits against po-

tential risk of severe, even fatal, reactions. The disease condition itself is unaltered by the drug. Use with caution in first trimester of pregnancy and in nursing mothers. Drug may appear in cord blood and breast milk. Serious, even fatal, blood dyscrasias, including aplastic anemia, may occur suddenly despite regular hemograms, and may become manifest days or weeks after cessation of drug. Any significant change in total white count, relative decrease in granulocytes, appearance of immature forms, or fall in hematocrit should signal immediate cessation of therapy and complete hematologic investigation. Unexplained bleeding involving CNS, adrenals, and G.I. tract has occurred. The drug may potentiate action of insulin, sulfonyleurea, and sulfonamide-type agents. Carefully observe patients taking these agents. Nontoxic and toxic goiters and myxedema have been reported (the drug reduces iodine uptake by the thyroid). Blurred vision can be a significant toxic symptom worthy of a complete ophthalmological examination. Swelling of ankles or face in patients under sixty may be prevented by reducing dosage. If edema occurs in patients over sixty, discontinue drug.

Precautions: The following should be accomplished at regular intervals: Careful detailed history for disease being treated and detection of earliest signs of adverse reactions; complete physical examination including check of patient's weight; complete weekly (especially for the aging) or an every two week blood check; pertinent laboratory studies. Caution patients about participating in activity requiring alertness and coordination, as driving a car, etc. Cases of leukemia have been reported in patients with a history of short- and long-term therapy. The majority of these patients were over forty. Remember that arthritic-type pains can be the presenting symptom of leukemia.

Adverse Reactions: This is a potent drug; its misuse can lead to serious results. Review detailed information before beginning therapy. Ulcerative esophagitis, acute and reactivated gastric and duodenal ulcer with perforation and hemorrhage, ulceration and perforation of large bowel, occult G.I. bleeding with anemia,

gastritis, epigastric pain, hematemesis, dyspepsia, nausea, vomiting and diarrhea, abdominal distention, agranulocytosis, aplastic anemia, hemolytic anemia, anemia due to blood loss including occult G.I. bleeding, thrombocytopenia, pancytopenia, leukemia, leukopenia, bone marrow depression, sodium and chloride retention, water retention and edema, plasma dilution, respiratory alkalosis, metabolic acidosis, fatal and nonfatal hepatitis (cholestasis may or may not be prominent), petechiae, purpura without thrombocytopenia, toxic pruritus, erythema nodosum, erythema multiforme, Stevens-Johnson syndrome, Lyell's syndrome (toxic necrotizing epidermolysis), exfoliative dermatitis, serum sickness, hypersensitivity angitis (polyarteritis), anaphylactic shock, urticaria, arthralgia, fever, rashes (all allergic reactions require prompt and permanent withdrawal of the drug), proteinuria, hematuria, oliguria, anuria, renal failure with azotemia, glomerulonephritis, acute tubular necrosis, nephrotic syndrome, bilateral renal cortical necrosis, renal stones, ureteral obstruction with uric acid crystals due to uricosuric action of drug, impaired renal function, cardiac decompensation, hypertension, pericarditis, diffuse interstitial myocarditis with muscle necrosis, perivascular granulomata, aggravation of temporal arteritis in patients with polymyalgia rheumatica, optic neuritis, blurred vision, retinal hemorrhage, toxic amblyopia, retinal detachment, hearing loss, hyperglycemia, thyroid hyperplasia, toxic goiter, association of hyperthyroidism and hypothyroidism (causal relationship not established), agitation, confusional states, lethargy; CNS reactions associated with overdosage, including convulsions, euphoria, psychosis, depression, headaches, hallucinations, giddiness, vertigo, coma, hyperventilation, insomnia; ulcerative stomatitis, salivary gland enlargement. (B)98-146-800-F (10/71)

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Indications: Effective in all types of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings and/or early morning awakening; in patients with recurring insomnia or poor sleeping habits; and in acute or chronic medical situations requiring restful sleep. Since insomnia is often transient and intermittent, prolonged administration is generally not necessary or

recommended.

Contraindications: Known hypersensitivity to flurazepam HCl.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. Caution against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Use in women who are or may become pregnant only when potential benefits have been weighed against possible hazards. Not recommended for use in persons under 15 years

of age. Though physical and psychological dependence have not been reported at recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage.
Precautions: In elderly and debilitated patients, initial dosage should be limited to 15 mg to preclude oversedation, dizziness or ataxia. If combined with other drugs having hypnotic or CNS-depressant effects, consider potential additive effects. Employ usual precautions in patients who are severely depressed, or with



depression or suicidal tendencies. Periodic blood counts and liver and kidney function tests are advised during prolonged therapy. Observe usual precautions in presence of impaired renal or hepatic function.

Side Reactions: Dizziness, drowsiness, lightheadedness, staggering, ataxia, falling have occurred, particularly in elderly or debilitated patients. Severe drowsiness, lethargy, disorientation and coma probably indicative of drug intolerance or overdosage, have been reported.

Also reported were headache, heartburn, upset stomach, nausea, vomiting, diarrhea, constipation, GI pain, nervousness, talkativeness, apprehension, irritability, weakness, palpitations, chest pains, body and joint pains and GU complaints. There have also been rare occurrences of sweating, flushes, difficulty in focusing, blurred vision, burning eyes, faintness, hypotension, shortness of breath, pruritus, skin rash, dry mouth, bitter taste, excessive salivation, anorexia, euphoria, depression, slurred speech,

confusion, restlessness, hallucinations, and elevated SGOT, SGPT, total and direct bilirubins and alkaline phosphatase. Paradoxical reactions, e.g., excitement, stimulation and hyperactivity, have also been reported in rare instances.

Dosage: Individualize for maximum beneficial effect. *Adults:* 30 mg usual dosage; 15 mg may suffice in some patients.

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Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, A has classified the indications as follows:

Possibly* effective: Contact or atopic dermatitis; impetiginized eczema; nummular eczema; infantile eczema; endogenous toxic infectious dermatitis; stasis dermatitis; pyoderma; chalcid eczema and chronic eczematoid otitis externa; acne cicatricata; localized or disseminated neurodermatitis; lichen simplex chronicus; anogenital pruritus (vulvae, scroti, ani); folliculitis; bacterial dermatoses; mycotic dermatoses such as tinea (capitis, cruris, corporis, pedis); moniliasis; intertrigo. A classification of the less-than-effective indications requires further investigation.

CONTRAINDICATIONS

Sensitivity to Vioform-Hydrocortisone, or any of its ingredients; untreated lesions of the eye; tuberculosis of the skin; viral skin lesions (including herpes simplex, vaccinia, and molluscum).

WARNINGS

This product is not for ophthalmic use.

In the presence of systemic infections, appropriate systemic anti-infectives should be used.

Use in Pregnancy

Although topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use in pregnant females has not been established. Therefore, they should not be used extensively on pregnant patients in large amounts or for prolonged periods of

PRECAUTIONS

May prove irritating to sensitized skin in rare cases. If this occurs, discontinue therapy. May stain.

If used under occlusive dressings or for a prolonged period, watch for signs of pituitary-adrenal axis suppression.

May interfere with thyroid function tests. Wait at least one month after discontinuance of therapy before performing these tests. The ferric chloride test for phenylketonuria (PKU) can yield a false-positive result if Vioform is present in the diaper or urine.

Prolonged use may result in overgrowth of nonsusceptible organisms requiring appropriate therapy.

ADVERSE REACTIONS

Few reports include: Hypersensitivity, local burning, irritation, pruritus. Discontinue if untoward reaction occurs. Rarely, topical corticosteroids may cause striae at site of application when used for long periods in intertriginous areas.

DOSAGE

Apply a thin layer to affected areas 3 or 4 times daily.

HOW SUPPLIED

Cream, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearyl alcohol, spermaceti, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of 5 and 20 Gm.

Ointment, 3% iodochlorhydroxyquin and 1% hydrocortisone in a petrolatum base; tubes of 5 and 20 Gm. **Lotion**, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearic acid, cetyl alcohol, lanolin, propylene glycol, sorbitan trioleate, polysorbate 60, triethanolamine, methylparaben, propylparaben, and perfume Flora in water; plastic squeeze bottles of 15 ml. **Mild Cream**, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a water-washable base containing stearyl alcohol, spermaceti, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of 1/2 and 1 ounce. **Mild Ointment**, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a petrolatum base; tubes of 1/2 and 1 ounce.

Consult complete product literature before prescribing.

CIBA Pharmaceutical Company
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Vioform-[®] Hydrocortisone (iodochlorhydroxyquin and hydrocortisone)

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TONSILLECTOMIES AND ADENOIDECTOMIES: ARE THEY REALLY NECESSARY?

Sylvan E. Stool, MD

William R. Mast, MD

Tonsillectomy, performed by surgeons for over 2500 years, is still an intensely stimulating and controversial procedure. Currently physicians offer a great variety of opinions and even the lay press devotes increased space regarding indications for surgery. The spectrum of medical opinion ranges from the ultra-conservative view that cancer of the tonsil or heart failure from upper airway obstruction are the sole indications while the most surgically aggressive practitioners feel that large tonsils constitute a foreign body that should be removed.

While tonsillectomy is a very old procedure, adenoidectomy is a comparative recent development. During the past century, removal of "adenoid vegetations" was developed and the combined procedure of tonsillectomy and adenoidectomy (T & A) popularized. The performance of these combined procedures paralleled the development of anesthesia and fluid replacement techniques and increased in incidence early this century.

We are now in the era of re-appraisal of T & A for a variety of reasons. The expense of two million procedures a year is considerable, and the mortality and morbidity are not insignificant. We are all concerned with peer review and quality control and the many new aspects of liability. Antibiotics have altered the course and incidence of many diseases and complicated the evaluation of a surgical approach.

The purpose of this article is to review some of the literature available on T & A, examine some of the opinions and concepts regarding this procedure and express an opinion regarding the indications for surgery.

There have been few controlled studies regarding these procedures. Only one large study was performed in the United States 50 years ago, two in England,

and one in New Zealand. These studies have been quoted and misquoted numerous times in the medical literature depending on the facet the author was trying to emphasize. A recent review summarizes the deficits of these studies and proposes a method for the conduct of a valid clinical study (1). A major problem in previous studies is the transient nature of the population, and it may be that an island population such as Puerto Rico would be the ideal place to conduct such a study. Another author states "the human and health care dimensions of T & A are so great, and its present status so confused and unsatisfactory, that the need for resolution seems compelling".

A recent article entitled "Ritualistic Surgery — Circumcision and Tonsillectomy" emphasizes some interesting facets of tonsillectomy and is of great value in putting the problem in its proper perspective (2). This article states that ritualistic surgery is performed on a non-scientific basis. Tonsillectomy has survived all these years while many other procedures that were thought to be "scientific" were discarded. Extreme examples of these are celiac ganglionectomy for cystic fibrosis and carotid-jugular shunts for mental retardation. These procedures were designed to treat hopeless conditions and abandoned as they were obviously not effective. The pressure to do something is always present in an exasperating circumstance, and this may be the situation with the child who is referred for T & A.

The interpersonal relationships developed around the "T & A problem" are very complex. A review of the role of the parties involved with the patient, their aspirations, expectations and ability will be briefly examined.

The child's physician usually wants his patients to remain well or wants to effect a rapid cure. The child with repeated respiratory viral illness or unrecognized allergy and in whom there does not seem to be an effective means of therapy may be felt to be a candidate for surgery or the physician may seek another opinion in response to the parent's anxiety

From the Departments of Otorhinolaryngology of the Children's Hospital of Philadelphia and the University of Pennsylvania School of Medicine.

Presented before the Annual Meeting of the Pediatric Section of the Puerto Rico Medical Association and the Puerto Rico Chapter of the American Academy of Pediatrics, San Juan, Puerto Rico, February 1973.

regarding the illness. In many instances the referring physician picks the surgeon according to the opinion he wants to get. He may refer the patient long distances to a surgeon he knows will hesitate to operate and thus retain control of the situation while satisfying the patient's demand for surgical intervention. He also may refer a patient with the idea that the surgical procedure is a technical exercise like ordering laboratory work and expect the surgeon to perform. Many physicians operate between these two extremes, but it is infrequent that the referring physician, who has much knowledge regarding the patient's condition, communicates this to the surgeon.

The surgeon — usually does not know the patient well and must decide whether the operative risk justifies the gain. He may not know the referring physician and what his expectations and ability are and usually has only a short-term follow-up on any of his patients. A much more difficult problem is the parent who independently seeks the services of a surgeon. The parent may withhold or magnify information according to his desire. When faced with these "doctor shoppers", the surgeon may well decide that he is as technically well qualified to do the surgery as the next colleague to whom the patient will undoubtedly go if he refuses surgery, and will consent to perform a non-indicated T & A.

A frequent comment made by various specialists is that the care the patient receives is predicated on economic consideration; hence the physician prescribes medication and the surgeon performs surgery. These considerations are difficult to document and evaluate but in all probability do not play a major role in decision making. The most fruitful method of approaching the problem would be an open dialogue between the physician and surgeon.

The parent — may see the illness in a much different light than the physician who is seeing numerous patients in the community with the same illness and who does not feel the patient is unusual. The inconvenience, expense, and stigma of having a child with multiple respiratory infections has always been difficult for parents. These problems are accentuated in the socio-economic situation where the mother frequently works and has a career of her own. She often will demand surgery as an obvious solution. On the other hand the child who has adequate indications for surgical therapy may not receive it because of the parents' fear or distrust of the physician, resulting in the previously mentioned doctor-shopper who becomes confused and alienated to the profession. There is clearly a need to acquaint parents to the usual pattern of

respiratory disease in children and prepare them for this era in a child's life.

The role of grandparents — is sometimes significant. Many people in this time of life forget the pattern of illness they saw in their children. The referral of a patient after a grandmother has spent a night in the house is not uncommon. A grandmother will tolerate her husband's snoring for years in resigned silence, but will listen to a snoring grandchild, become alarmed, and initiate referral to a surgeon. If the child, in addition, is going through a period of physiological anorexia, then the relation of snoring, poor appetite and "large tonsils" may further emphasize the need for surgical intervention.

Teachers, friends, and school physicians frequently pressure physicians "to do something". The school systems are charged with health evaluation and not infrequently a normal child with lymphoid hyperplasia may be referred for consideration of T & A. There is much need for education of the school health personnel regarding normal development. The school hearing programs in general have been an important part of health care and do provide a service that would otherwise not be available. Friends of a family who have a child with respiratory illness may occasionally be of great help, however, more often they tend to add to the confusion. In general, they remember only the positive aspects of surgical therapy and forget the child who had complications or did not improve.

The patient is a child and most children like to feel well. However, even some young children seek the secondary gain from special care given during illness and increased attention because of a planned surgical procedure even though this may not always be apparent. Occasionally an older child or adolescent may recognize that repeated illness is detrimental and if he has recurrent tonsillitis, he himself may request surgical intervention. He frequently is correct.

Little has been said about the contraindications for surgery, and this may be the most important aspect to explore. Obviously one should avoid operating on a patient who has a marked bleeding tendency or another major medical disorder. Also not obvious are those children who may be using this tissue for speech production. Specifically, you must spot the child who has marginal velopharyngeal closure and in whom the removal of adenoid tissue will result in a speech deformity simulating that seen with cleft palate and hearing loss from serous otitis (Figs. 1 and 2). This child may be unable to communicate and become labeled as retarded or a behavior problem (3).

"Are there any indications for T & A?" was the

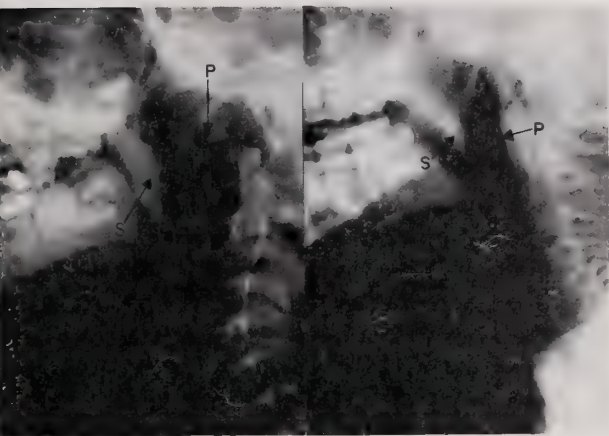


Fig. 1: Radiographic examination of the nasopharynx in the evaluation of velopharyngeal incompetence necessitates lateral neck x-rays, a technique available in most radiology departments. A, (left) shows a normal subject producing the test sound Mm. The soft palate (s) is anterior to the pharyngeal wall (P) creating a wide nasopharyngeal isthmus. B, our patient with velopharyngeal incompetence demonstrates the same normal relationships while phonating Mm. However, the palate is short and cannot touch the posterior pharyngeal wall as the adenoid has been removed.

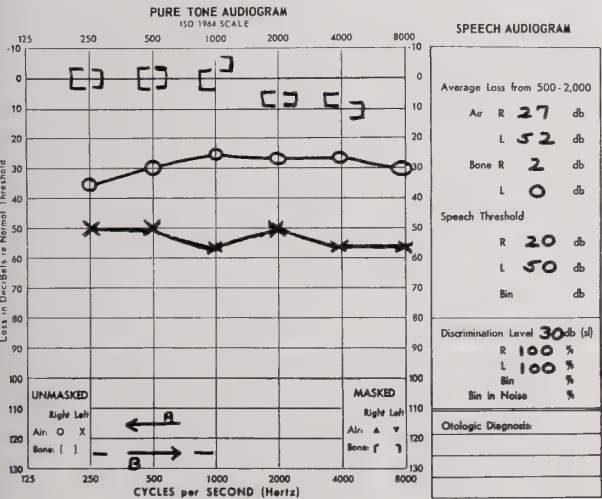


Fig. 2: An audiogram of a patient with marginal velopharyngeal closure who had recently undergone an adenoidectomy with subsequent development of a serous otitis media.

subject of this presentation suggested by the Pediatrics Section and the Academy of Pediatrics Chapter. The answer is a qualified "Yes". First the procedures should be considered as independent operations.

Tonsillectomy or Adenoidectomy or Tonsillectomy and Adenoidectomy. The opinions of the authors

represent their practice and experience and in view of the lack of controls may not be more valid than any other physicians (4). The procedures must be approached as symptomatic therapy and with the attitude: Does the symptom justify the risk of therapy and are alternate methods of therapy satisfactory. Thus the indications may be compared with the lights of a traffic signal.

(a) Green - Surgery indicated

Those patients who have cardiac failure on the basis of obstruction deserve tonsillectomy or adenoidectomy or both. The choice will depend on the surgeon.

(b) Yellow - Caution

Peritonsillar abscess - Patients with recurrent febrile tonsillitis who do not respond to usual antibiotic therapy, who do not have systemic disease and are preferably over the age of six years. Mouth breathing and snoring are some minor considerations and usually do not constitute an indication for surgery. Recurrent otitis media in the infant or young child can usually be managed with myringotomy although this procedure with adenoidectomy may have some value. In general, for the treatment of otitis myringotomy seems the most direct approach.

(c) Red - Surgery contraindicated in those instances when the risk outweighs the benefits and when removal of these tissues may result in impairment of the speech mechanism.

Summary

There is currently much divergence of opinion regarding the indications for tonsillectomy and adenoidectomy, which should be regarded as two separate procedures with specific indications for each. Involved in the decision for or against surgery is a complex interaction between many parties, including the child, the parents and grandparents, the referring physician, the surgeon, and even school officials. The benefits of the procedure must be constantly weighed against the risks involved. Special note must be paid to those children with marginal velopharyngeal closure.

Resumen

Existe actualmente mucha divergencia de opinión en cuanto a las indicaciones para amigdalectomía palatina y adenoidectomía. Estas deben ser consideradas operaciones diferentes con indicaciones específicas para cada

una. La decisión a favor o en contra de la operación involucra una compleja interacción entre muchas partes, incluyendo al niño, sus padres y abuelos, el médico de cabecera, el cirujano y hasta funcionarios escolares. Los beneficios de la operación deben ser constantemente pesados contra los riesgos que la misma conlleva. Debe prestársele particular atención a niños afectados por oclusión marginal velofaríngea.

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FALSE ELECTROCARDIOGRAPHIC PATTERNS OF MYOCARDIAL INFARCTION IN CHRONIC PULMONARY EMPHYSEMA AND CHRONIC COR PULMONALE

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Chronic obstructive lung disease (COLD) may be associated with coronary atherosclerosis and myocardial infarction (MI), particularly in view of the fact that atherosclerotic coronary artery disease is the most frequent type of heart disease, while pulmonary heart disease ranks fourth in prevalence (1), comprising 9-10 percent of autopsied cases of heart disease (2); more than two-thirds of the pulmonary emphysema (PE) population exceeds 60 years of age, and coronary artery disease (CAD) is also frequent in the aging population (3).

Some have claimed that chronic diffuse pulmonary disease predisposes to or accelerates the development of CAD, while other workers have found MI to be relatively infrequent in patients with PE and often clinically "silent" when it did occur; these latter findings were attributed to an improved anastomotic circulation and coronary artery dilatation induced by chronic hypoxia. Twenty-one percent of one series of men with pneumoconiosis died from CAD. Another study revealed that patients with chronic diffuse pulmonary disease have neither a higher nor lower prevalence of MI or ischemic electrocardiographic changes (4, 5, 6, 7, 8). One interesting study revealed that coronary heart disease could be accurately diagnosed from the electrocardiogram (ECG) in 84 percent of patients showing coronary atherosclerotic lesions at autopsy, while the diagnostic accuracy in pulmonary heart disease was 72 percent; but when both coronary and pulmonary heart diseases were present the accuracy was only 55 percent; when neither were present, 68 percent. The accuracy for all four groups was 71.5 percent (5). So, in view of these controversial findings, the diagnosis in any individual patient may be difficult.

A host of conditions other than MI have been recognized as causing "electrocardiographic patterns" (Q waves, QS and QR complexes) resembling those of infarction. COLD and chronic cor pulmonale (CP) are among these, as well as acute CP (acute pulmonary

embolism). This relationship was noted many years ago by Zuckermann and associates (1948) (9), and appreciated by other early observers — Myers (1950) (10), Sodi-Pallares and associates (1952) (11), etc. These patterns have been referred to by some as the pseudo-anterior and pseudo-diaphragmatic infarction patterns of chronic PE and CP. In spite of this previous recognition, one continues to encounter patients with COLD in whom the diagnosis of MI has been made on the basis of certain electrocardiographic features alone.

This article reviews this interesting relationship and presents 18 patients who offer this clinical and electrocardiographic dilemma.

Materials

Eighteen patients with COLD were presented. ECG's and Frank vectorcardiograms (VCG's) were obtained and analyzed. These were classified according to the main site of pseudo-infarction. The VCG's were obtained by the same method and equipment as previously described (12). The diagnoses of COLD and CP were based upon the clinical history and physical examination, routine laboratory data, chest x-rays, ECG's, and in certain instances blood gases and pulmonary function studies. Patients considered on this information to have coronary heart disease or other types of heart disease were excluded. None of the patients had coronary arteriography. In two cases there was autopsy confirmation.

Results

Of the 18 cases, 10 were classified as pseudoanterior-septal, 1 pseudoanterior, 1 as pseudoanterolateral, 4 as pseudoanteroseptal lateral, 1 as pseudodiaphragmatic and 1 as pseudodiaphragmatic anterolateral MI. Some of the patterns resembled other patterns; thus the divisions are not sharply delineated.

Case 1 was a chronic smoker and had a history of asthma since 20 years of age. Chest pain was recorded. The arterial PCO_2 had been elevated (74, > 124 mm Hg). ECG's showed QS complexes in V_1 and a q wave in V_{2-4} (on another tracing). He had had digitalis intoxication (atrial tachycardia with block). The xiphoid and V_{2-6} th IS level leads showed q waves while the V_1 -5th IS lead showed a QS complex. The VCG demonstrated absent initial anterior

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forces in the horizontal (H) plane, a variable P form in lead Y, and only a microscopic r wave in lead Z. There appeared to be small anterior forces in the right sagittal (RS) plane.

Case 2 showed low r waves in the right precordial leads; r waves were present in lower leads. Definite, small anterior forces were present, as seen in the H and RS planes of the VCG, and in the Z orthogonal lead (Q wave).

Small r waves were evident in the right precordial leads of Case 3, while the VCG revealed definite small initial forces and right ventricular hypertrophy (RVH).

Case 4 had no history of chest pain. QR complexes or Q waves were present in the right precordial and right chest leads. Anterior forces were practically absent.

The r waves in leads V_{1-3} of Case 5 were variably present. Anterior forces were normal, except that the H plane showed small initial anterior forces (loop).

Case 6 showed QS complexes or Q waves in V_{1-3} .

Case 7 was different in that right bundle branch block (RBBB) was present, as was right axis deviation. "Chronic ASHD" had been one of the clinical diagnoses. Small r waves with block, atrioventricular dissociation with junctional rhythm and ventricular bigeminy (not shown) were probably due to digitalis intoxication. Autopsy confirmed the clinical diagnoses of chronic CP, chronic bronchitis, PE, bronchiectasis, pulmonary and pleural fibrosis, and tracheobronchomegaly. No MI was present and the coronary arteries were patent; no atheromatous plaques were seen. The myocardium was red and firm. The measurements of the right atrium (RA), right ventricle (RV), left atrium (LA) and left ventricle (LV) were: 0.1 cm., 0.8 cm., 0.1 cm., and 1.5 cm. in thickness, respectively.

Case 11 had a left fibrothorax with the heart deviated to the left chest. "Infarction-like" changes were present in the anterior and lateral leads; another tracing revealed qR complexes in V_{1-3} , or QS/tiny r in V_{2-6} .

The ECG of Case 12 suggested an antero-septal-lateral MI. Q waves or QR complexes were evident in the right chest leads; low chest leads showed only tiny r or QS complexes. This patient (Case 13) with asthma since childhood, had an ECG that was classified the same as that of the previous patient.

History was limited in Case 14 (probably a coal miner). The ECG mimicked an old diaphragmatic infarction; qR complexes were present in the right chest and low V_1 leads.

The r waves of Case 15 were small from V_{1-3} and in AVL (QR). There were small initial anterior and rightward forces on the VCG.

Case 16 presented low r waves from V_{1-5} ; r waves were also low in the right chest and the low chest leads; lead I sign (almost qR complexes) were present in V_{1-4} and a QS complex with negative P wave in lead AVL. Autopsy showed no MI, but right atrial enlargement, RVH and CP.

Small r waves in V_{1-4} , with inverted T waves in V_{2-4} , and a QS complex with an inverted P wave in AVL, were seen in Case 8.

The ECG of Case 9, a coal miner, revealed q waves in the right precordial and right chest leads, and QS complexes in leads I and AVL. Non-paroxysmal junctional tachycardia.

This interesting patient's (Case 10) ECG demonstrated QS complexes or only tiny r waves in leads I, AVL and V_{1-3} . Practically no anterior forces were evident either by the

VCG loops or by the orthogonal Z leads. Atrial tachycardia present. Definite initial anterior forces were evident.

Almost QS complexes (small voltage) were present in leads I and AVL of Case 17, with qR complex in V_1 , q waves in V_{2-5} and an rS complex in V_6 . Interestingly, the VCG showed a mainly anterior QRS loop with some early leftward forces (Type A RVH). Complex arrhythmias. This patient had an apical systolic murmur, pheraps of rheumatic etiology.

It is very difficult to exclude additional MI in this elderly male whose ECG mimicked a diaphragmatic-anterolateral MI; his tracings did not change over at least a 2 year period. Only tiny initial anterior and rightward forces were demonstrated.

Eight of the patients had been smokers. Three of the patients had complained of some type of chest pain. Six of the patients developed increases of the arterial PCO_2 level.

VCG QRS loops were located as follows: 6 were posteriorly and partly or mainly to the right; 1 posteriorly and leftward; 1 posteriorly; and only 1 QRS loop (Case 17) was located mainly anterior.

Discussion

Certain cases of COLD manifest ECG's which are suggestive of or compatible with myocardial infarction. This is not always appreciated by the attending physician, thus leading to grave diagnostic, therapeutic and prognostic errors. On the other hand, a COLD pattern may not only mimic, but may mask a MI; both of these conditions may be present in a single patient (13).

Zuckermann and associates, in 1948, reported the ECG's in 50 cases of chronic CP without MI; in 36 percent of these cases, there was a QS or W-shaped QRS complex, or a deep Q wave in the right precordial leads (9). Myers, in his early classic publications, emphasized electrocardiographic patterns of septal and/or anterior wall infarction (precordial leads) in patients with RVH or right ventricular dilatation; COLD was among the causes (10). In Mounsey and colleagues' study of patients with severe PE, QR or QS complexes were seen in leads V_4R , V_6R and V_1 (their patterns VI and VIII). (14). Fowler and Helm, in 1953, published three cases of CP which demonstrated posterior initial vectors; two cases had a q wave in the right precordial leads (15).

Many subsequent publications have emphasized this interesting phenomenon (5, 11, 13, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29), or at least shown electrocardiographic illustrations depicting these patterns.

An early publication of the group of Sodi-Pallares noted that acute and chronic CP could sometimes manifest qR or QR type complexes in the right precordial leads in the absence of MI (11); this was attributed to hypertrophy or dilatation of the right

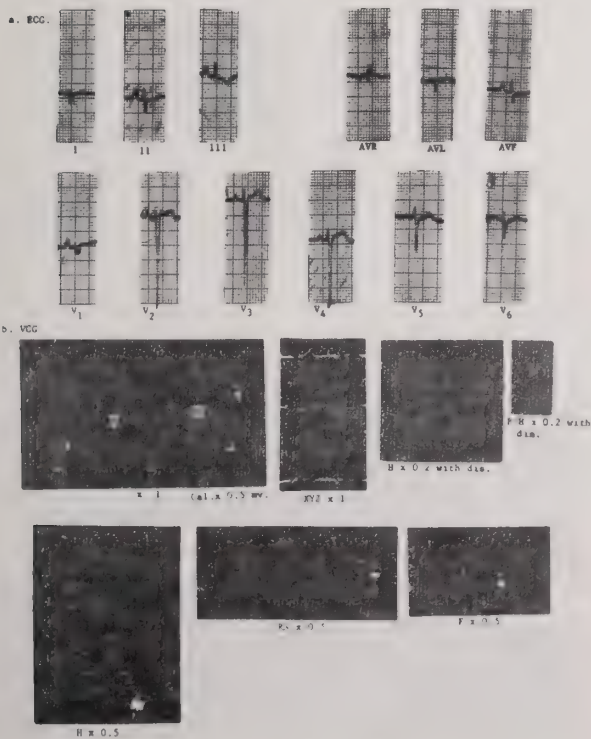
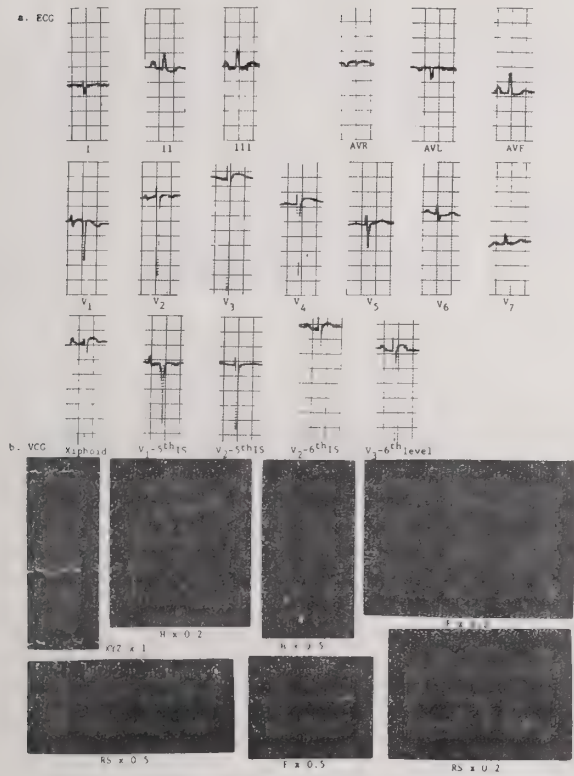


Fig. 3: Case 3. 60 y.o. F. "Pseudo-anteroapical" MI. Chronic obstructive pulmonary disease; fibrosis. Cor pulmonale (RVH type C). Congestive heart failure. History of pneumonias and pulmonary tuberculosis.

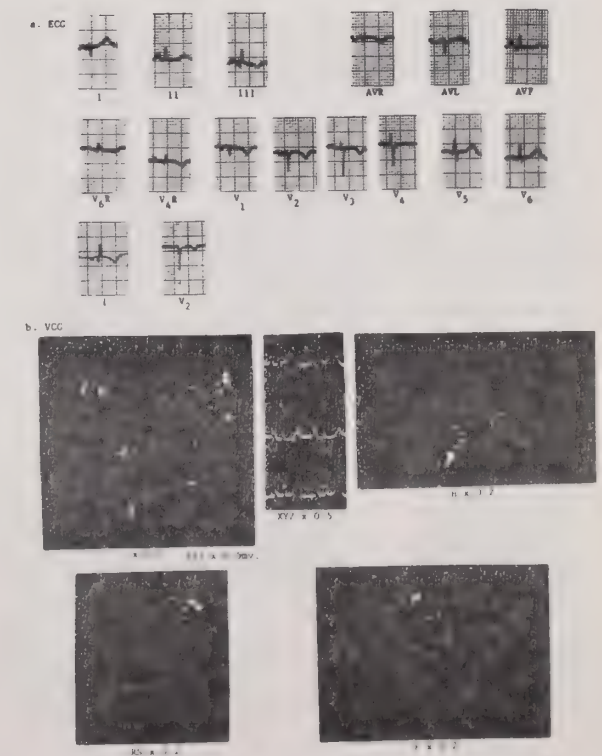
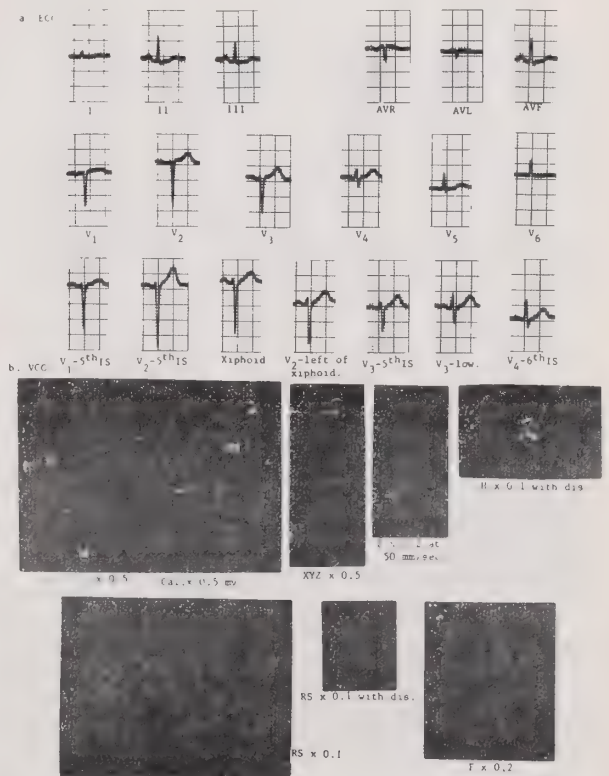


Fig. 4: Case 4. 58 y.o. F. "Pseudo-anteroapical" MI. Severe chronic obstructive lung disease; emphysema; cor pulmonale. Congestive heart failure. History of pneumonias.

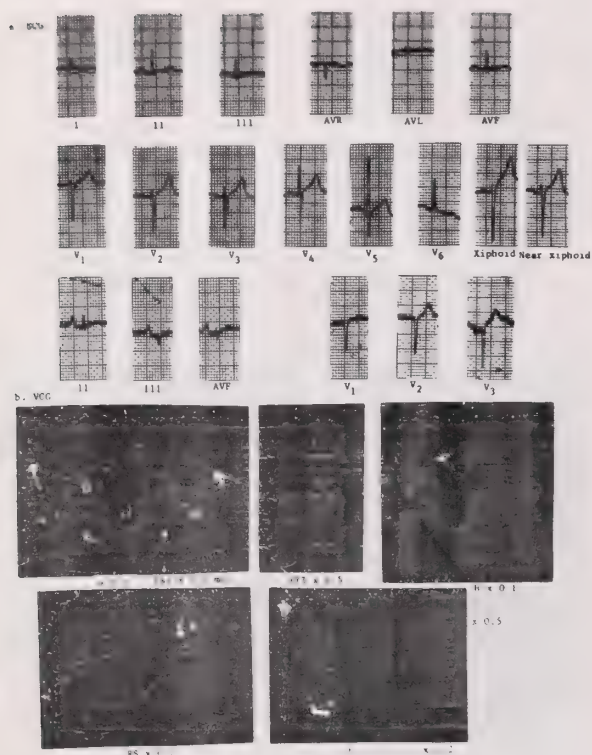


Fig. 5: Case 5. 77 y.o. M. "Pseudo-antero-septal" MI. Chronic pulmonary emphysema.

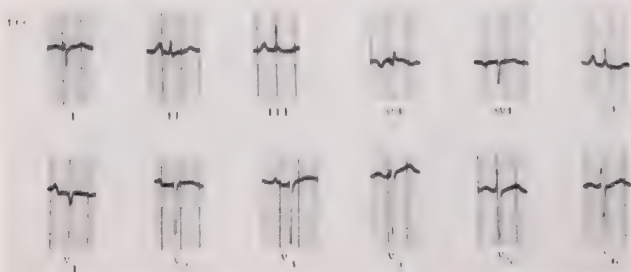


Fig. 6: Case 6. 68 y.o. F. "Pseudo-antero-septal" MI. Chronic obstructive and restrictive lung disease with severe emphysema and fibrosis. Cor pulmonale. Congestive heart failure.

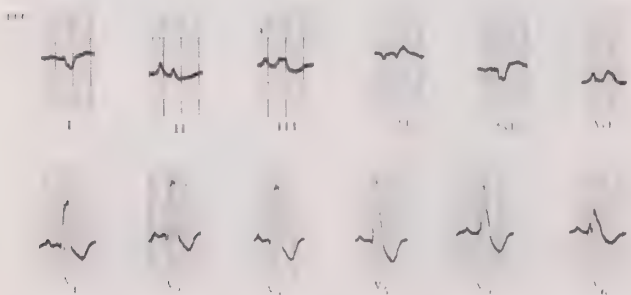


Fig. 7: Case 7. 65 y.o. M. "Pseudo-antero-septal" MI. Chronic pulmonary emphysema. Cor pulmonale. Congestive heart failure. RBBB. RAD.

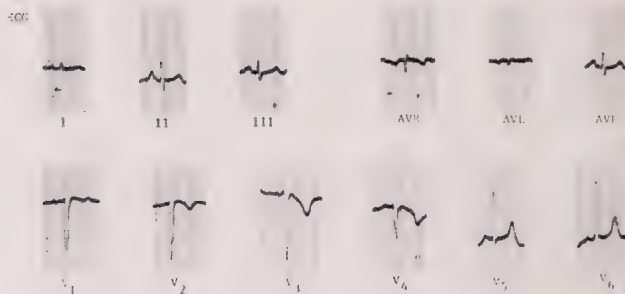


Fig. 8: Case 8. 63 y.o. M. "Pseudo-antero-septal" MI. Chronic pulmonary emphysema and fibrosis. Bronchiectasis.

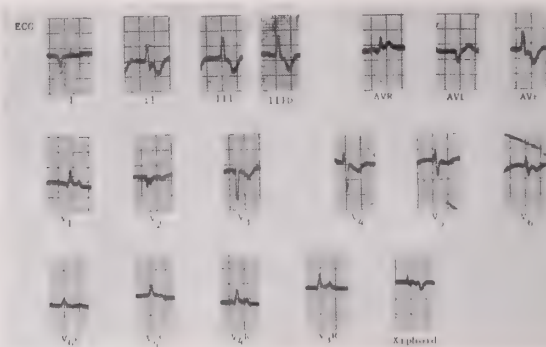


Fig. 9: Case 9. 72 y.o. M. "Pseudo-antero-septal" MI. Chronic pulmonary emphysema. Acute and chronic cor pulmonale. Arrhythmia. Pneumonia. Anthraco-silicosis.

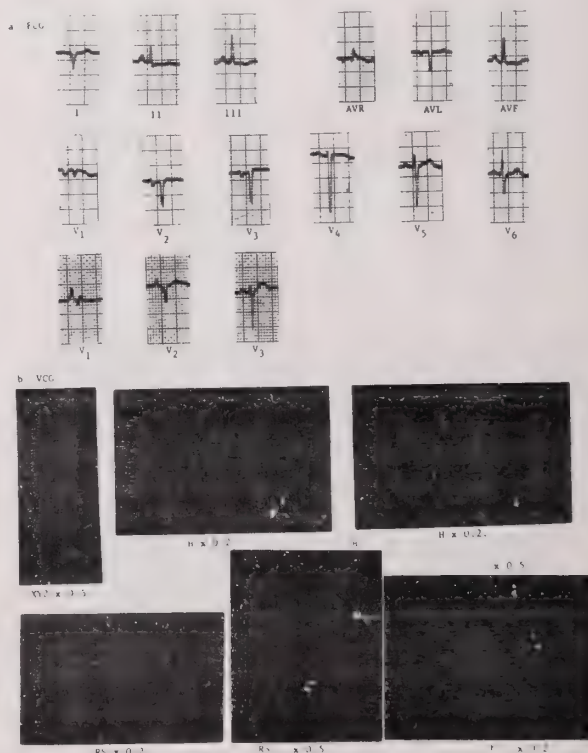


Fig. 10: Case 10. 48 y.o. F. "Pseudo-antero-septal-lateral" MI. Severe chronic pulmonary emphysema, fibrosis, and cor pulmonale. Pneumonias. Congestive heart failure. Mounier-Kuntz disease.

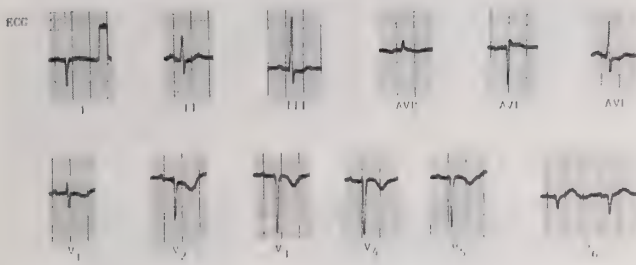


Fig. 11: Case 11. 51 y.o. F. "Pseudo-anterolateral" MI. Pulmonary emphysema and fibrosis. Chronic cor pulmonale. Left fibro-thorax. Pneumonia. Congestive heart failure. Pulmonary tuberculosis-old and active. Cerebro-vascular accident.

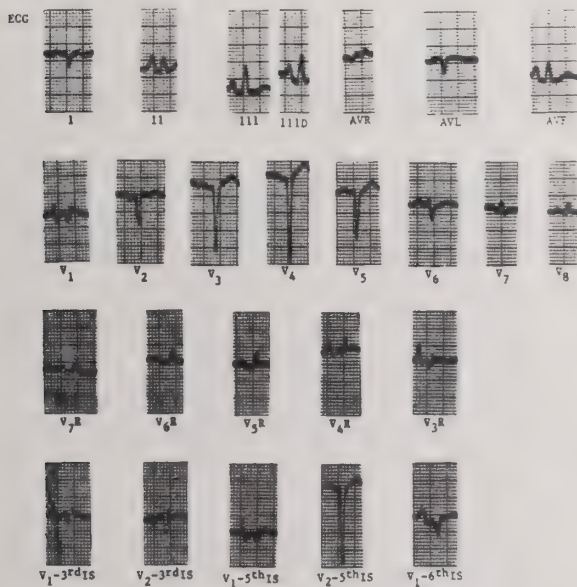


Fig. 12: Case 12. 65 y.o. M. "Pseudo-anteroseptal-lateral" MI. Chronic pulmonary disease and cor pulmonale. Congestive heart failure. Anthraco-silicosis.

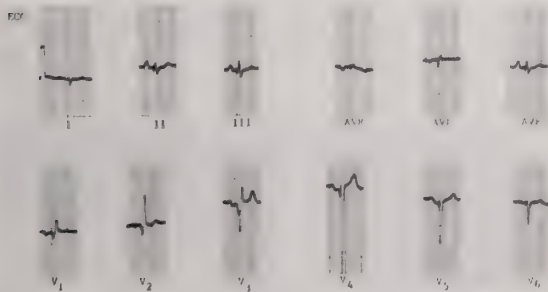


Fig. 13: Case 13. 58 y.o. F. "Pseudo-anteroseptal-lateral" MI. Chronic obstructive lung disease-emphysema. Cor pulmonale.

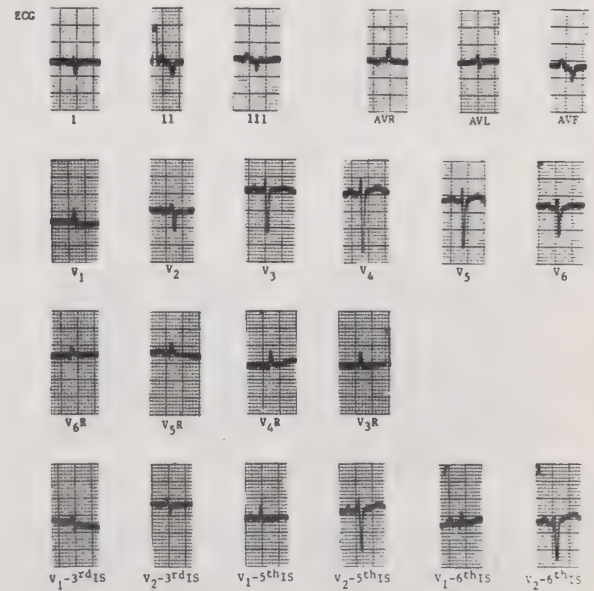


Fig. 14: Case 14. 63 y.o. M. "Pseudo-diaphragmatic" MI. Chronic lung disease. Cor pulmonale. Anthraco-silicosis.

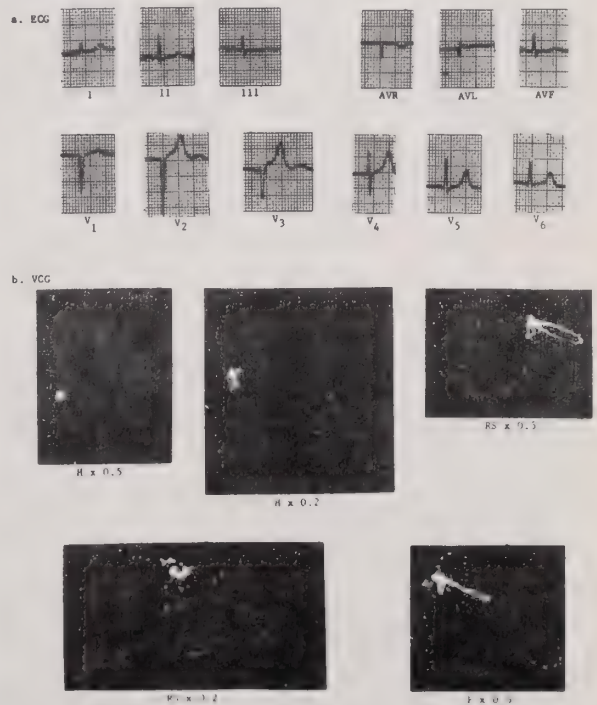


Fig. 15: Case 15. 53 y.o. M. "Pseudo-anteroseptal" MI. Severe chronic obstructive lung disease.



Fig. 16: Case 16. 66 y.o. M. "Pseudo-anterior" MI. Chronic obstructive lung disease and chronic cor pulmonale. "Asthma". Bronchiectasis, and pulmonary fibrosis. Congestive heart failure.

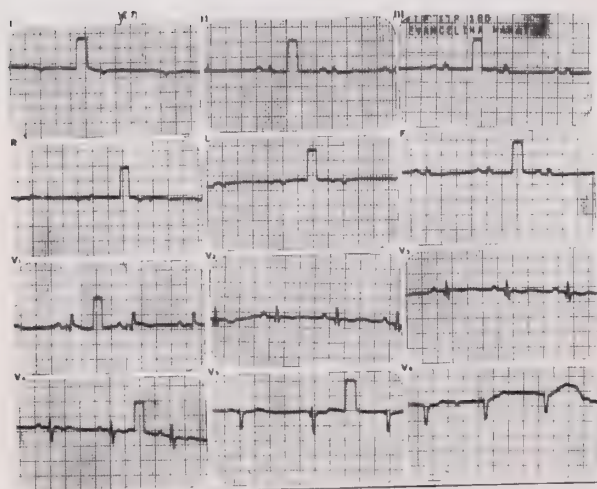


Fig. 17: Case 17. 45 y.o. F. "Pseudo-antero-septal-lateral" MI. Chronic obstructive lung disease and chronic cor pulmonale. History of bronchial asthma. Congestive heart failure.

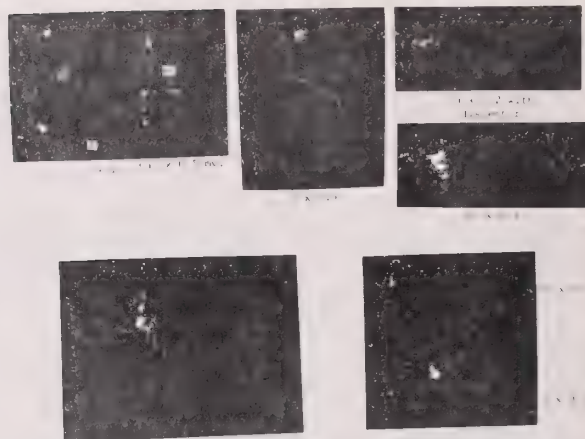


Fig. 18: Case 17. VCG of the same patient as in Fig. 17.

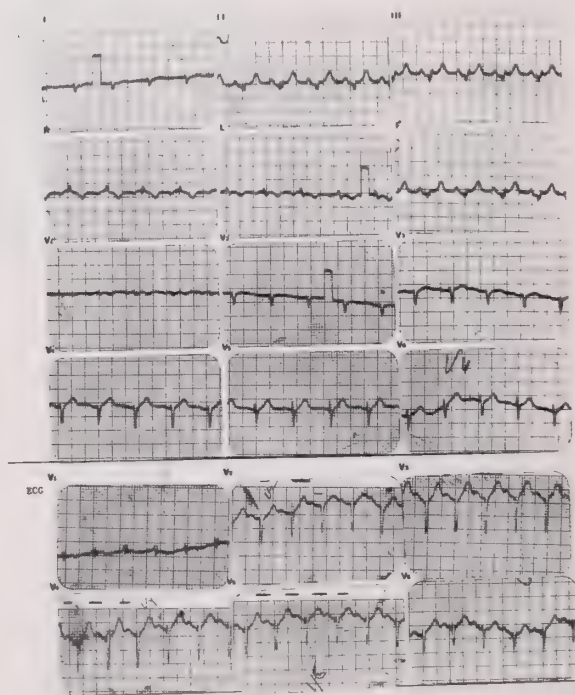


Fig. 19: Case 18. 83 y.o. M. Pattern of diaphragmatic-antrolateral MI's. Chronic lung disease. Above— 12-lead ECG. Below— precordial leads only (obtained on a different date).

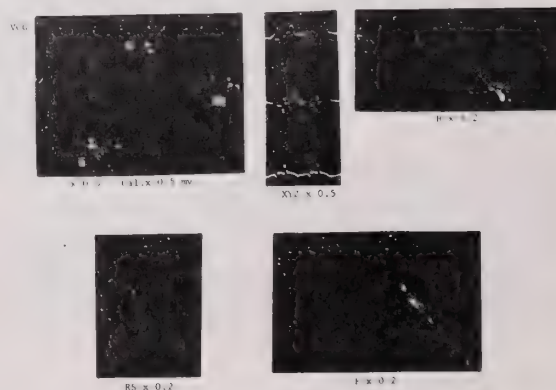


Fig. 20: Case 18. VCG of the same patient as in Fig. 19.

heart chambers. In RA dilatation the electrode was oriented toward the high interventricular septum and faces the electrical field of the septum through the "electric sink" formed by the large mass of blood in the dilated RA. This may resemble lead AVR; "atrialization of the ventricular complexes" (28). The genesis of a "q" wave in CP has been explained also by; activation of the crista supraventricularis, registration of LV potentials through a dilated RA, stimulation of the septum from right to left, and as representing the "s" of an rsR^1 pattern (29). Surawicz and colleagues observed QS and QR complexes in leads V_2 - V_4 (their figure 1), and believed that atypical spread of excitation or a change in the position of the electrode in respect to the heart accounted for this. Exploration by multiple chest and abdominal unipolar leads (ensiform and epigastric levels) and VCG's revealed that in almost all such cases, the vector of the initial portion of the QRS complex is directed downwards. So, in the absence of infarction, patients with this pattern almost invariably showed an initial R wave (rS) in leads recorded from positions below the standard level of V_3 and V_4 , and the initial 0.02 vector by VCG was inferior in 91 percent of subjects. The majority of patients with infarction and a similar electrocardiographic pattern showed Q waves (QS) in the lower leads, and 50 percent showed Q waves in ensiform or epigastric leads (16). Later workers attributed qR complexes in leads V_1 and V_2 to cardiac rotation on the long axis, bringing the posterior portion of the LV under these leads. A QS pattern could appear in lead AVF because with clockwise (cw) rotation the current of septal activation may be at right angles to this lead and what otherwise would be an rS (in a horizontal heart) becomes a QS complex (19).

In a 60-year old male with COLD and no MI (autopsied), Bernreiter observed deep Q waves in leads 11, 111 and AVF, which did not change over a 5-year period. These were explained by marked cw rotation of the heart around the longitudinal axis and posterior displacement of the apex. P waves were tall and peaked in these leads (20). Other similar cases have been illustrated. A QS complex with a negative T wave in V_{1-3} , and low QRS voltage may mimic an anteroseptal MI (21). Figure 18 in Burch and DePasquale's article suggests an anteroseptal-lateral MI (22). These "q patterns" have been utilized for the diagnosis of RVH in chronic CP (23) as follows: Fairly conclusive-qR, QR, qRs in leads V_4R , V_3R , and V_1 ; Strongly suggestive-QS, Qr or qr in V_{1-3} (in absence of anteroseptal

MI); Suggestive-"infarct" Q waves (0.04 sec. or more wide) in leads 11, 111 and AVF, in the absence of an inferior MI. These authors illustrated an axis illusion phenomenon with a false infarct pattern (the P waves and ST segments differed). A Q wave > 0.04 second (sec) wide was present in pulmonary heart disease in leads 1, 11, 111 and in AVF in 1 percent of cases each (5).

Figure 1 of Selvester and Rubin's report demonstrated severe emphysema and a pseudo-anteroseptal-lateral MI. They mentioned that an MI may mimic or mask the changes produced by emphysema, and that emphysema alone may mimic an MI; and hence, they believed that the electrocardiographic diagnosis of emphysema was hazardous in the presence of electrocardiographic evidence of an MI (13). In MI one can see posterior and superior QRS vector displacement with low voltage.

A QS pattern with absence of an initial R wave in the midprecordial leads was found in 4 of 15 subjects with CP and emphysema, and in no patients with CP due to idiopathic pulmonary hypertension or pulmonary thromboembolism. Posterior displacement of the QRS loop and perhaps downward displacement of the null plane so that the conventional precordial leads are recorded superior to this position, were suggested to be the causative factors (25).

Neal and associates stated that these q or qs waves in the right precordial leads may, in some instances, be the electrocardiographic evidence of true myocardial scarring, and that myocardial scarring had been found in about 50 percent of postmortem findings of this type of CP (28).

In a recent large series of patients (544) from India, with chronic CP, 17 percent presented a QS pattern in all chest leads. Right ventricular hypertrophy manifested as a qR with the R less than 5 mm. high in 39 percent and taller than 5 mm. in 16 percent of cases. Patterns of qR and incomplete RBBB interchanged freely in serial records and were sometimes present in the same record (29).

In 1960, Walsh and colleagues observed four QRS loop patterns (cube system) of patients with chronic CP due to emphysema. Their types B and C were characterized by abnormal initial vectors (small or decreased forces by VCG), manifesting as an r or qRs complex in lead V_1 (30). Subsequent workers depicted qR, QR and QS complexes in the right precordial and right chest leads, and abnormal initial H plane QRS vectors (also using the cube system of electrode placement), in 6 of a 100 patients with CP. However, no emphasis of these stimulating a MI was

made (31).

A 62-year old male with COLD (Case 3 of Moret et al) demonstrated an electrocardiographic axis of -110° and a QS complex in leads I, II, III and AVF. The vectorcardiographic loops (McFee and Parungao system) were located to the right, superiorly and posteriorly. The H plane loop rotated counterclockwise (ccw), as did the frontal (F) loop, with the initial forces going superiorly. Myocardial hypoxia was suggested as a cause (32).

Murata and co-workers reported 8 cases from 288 patients whose VCG and ECG indicated an old MI (prominent Q waves in V_2 and/or V_3). There was a high incidence of coronary sclerosis, scattered myocardial fibrosis in the false positive cases of MI at necropsy (no extensive myocardial disease was present). Neither were RVH, significant septal hypertrophy or giant RA found. They attributed this pattern to the high incidence of PE associated with an altered downward displacement of the heart, and possibly to abnormal intraventricular conduction. They too, were impressed with the incidence of significant Q waves simulating anteroseptal MI in patients with severe emphysema (33).

Type I, II and III of Brown (cube VCG) showed abnormal initial left and anterior vector orientations, while the T loop was located to the left and posteriorly in Types II and III (34).

The ECG's and cube VCG's of 72 patients with chronic PE were recently studied by Wachtel et al. Their Group IV patients (the largest group) was characterized by a posterior position of the cardiac vector, best appreciated in the H plane; this pattern revealed itself as Qs or r/S complexes in the precordial leads. A patient with emphysema and QS complexes in V_{1-3} suggesting an anteroseptal MI and/or hypertension, showed no left ventricular hypertrophy, RVH nor MI at post-mortem examination (their Figure 6). This pattern was believed to represent only rotation and displacement of the cardiac vector and not to be conclusive for RVH. They noted that a posterolateral MI may simulate RVH in a patient with emphysema (tall R waves in leads AVR, V_1 and r/S complex in V_6 with left axis deviation (LAD)). Their patients with emphysema all had cw or figure-of-8 F plane loops, and they believed that a ccw F loop or true LAD indicated associated left heart disease (35).

Computer analysis of orthogonal ECG's (Frank system) of 405 patients with moderate and severe emphysema revealed complete loss of the anterior forces in 21 percent of the cases and an abnormally low $Q:R_Z$ ratio in an additional 10 percent. The $Q:R_X$ and

$Q:R_Y$ ratios were abnormally large in about 7 percent of cases, thus mimicking lateral and diaphragmatic infarcts. Some correlation was found between these Q wave changes and arterial PCO_2 levels, suggesting that pseudo-infarct patterns were more likely to develop in advanced PE. The authors stated that MI could not be excluded completely, even without a history of chest pain or infarction. Of their 22 autopsied cases, 2 showed advanced and 8 moderate coronary artery atherosclerotic changes. Coronary disease was suggested by the presence of atrial fibrillation, in 11 percent of their cases (3).

Another publication by Pipberger's group from the Veterans Administration Cooperative Study was based upon digital computer technique studies of 1002 infarct patients and 405 emphysema patients, using Frank's corrected orthogonal lead system, placing the electrodes in the fourth intercostal space (36). In 30 percent of the emphysema group, an erroneous diagnosis of an anterior MI could have been made, while 11 percent of the group mimicked posterodiaphragmatic and 8 percent of the group lateral infarcts (Q waves in leads I, AVL, V_{5-6}), respectively. By using simple electrocardiographic hand measurements for differentiation these percentages could be reduced to 6 percent, 5 percent and 5 percent, respectively, while discriminant function analysis produced an additional improvement of 3 percent. Thus by these measures an original total of 50 percent of records simulating infarction, only 13 percent remained unclassified or questionable.

Differential parameters and loops were delineated. Absent Q waves in lead Z (20 percent), manifesting as QS complexes in V_{1-9} , or an abnormal low Q/R ratio in lead Z (10 percent), suggested anterior MI. This group demonstrated an increase in R peak time in X, a greater R voltage and duration in X and Z, a greater QRS maximum vector, with less anterior forces in the H and RS planes, and a loop more to the left in the H plane, than did the emphysema group. The diaphragmatic infarct group showed a deeper Q in Y and Z, a larger R in X, a smaller R and greater peak time in Y, and more superior forces, while the lateral MI group showed low amplitude R waves, deep Q waves and greater R peak time in lead X, with the QRS loops being displaced to the right and having a greater posterior maximum vector, than did the emphysema patients. The former group rotated cw in the H plane and ccw in the F plane, while the latter group rotated contrariwise to this (36).

Another recent study along the same lines demonstrated improved differentiation between anterior wall MI and COLD, using multivariate statistical analysis of four

VCG items [$R_x + R_z$, 25 msec. Z component, QRS duration, and $S_x / (S_x + R_x)$] and either two or four ECG items [$RV_6 + SV_1$, QRS duration, RV_4 and P in AVF] (37). One-fourth of the cases with COLD had reduced or absent initial, anteriorly directed QRS forces.

Emphysema causes a small QRS vectorcardiographic loop located to the left and posteriorly. Mitral stenosis may also produce a posteriorly oriented loop.

Although this study lacks the benefits of coronary arteriography (38), it does support many other publications and observations (including autopsy material) of the mimicking behavior of the ECG in COLD and chronic CP, wherein MI is simulated, thus leading to an entirely different approach to the management and prognosis of the patient.

Since the initial cases were collected, two cases of chronic CP and one of COLD with mimicry of an antero-septal MI, one case with PE and a probable pseudo-diaphragmatic infarction pattern and an "axis illusion phenomenon", and another possible additional case with RBBB and Q waves in the right precordial leads, have been seen.

Summary

This article emphasizes that chronic obstructive lung disease and chronic cor pulmonale may manifest electrocardiographic patterns that simulate myocardial infarction. The supporting medical literature is reviewed and 18 cases suggesting this mimicry are presented.

Resumen

Este artículo hace énfasis en cómo la enfermedad crónica obstructiva pulmonar y el cor pulmonale crónico simulan algunas veces patrones electrocardiográficos sugestivos de infarto del miocardio. Presentamos un repaso de 18 casos con este fenómeno sustanciado por la literatura médica actual en la materia.

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are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in postsympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Rarely, necrotizing vasculitis, paresthesias, icterus, pancreatitis, and xanthopsia have occurred with thiazides alone.

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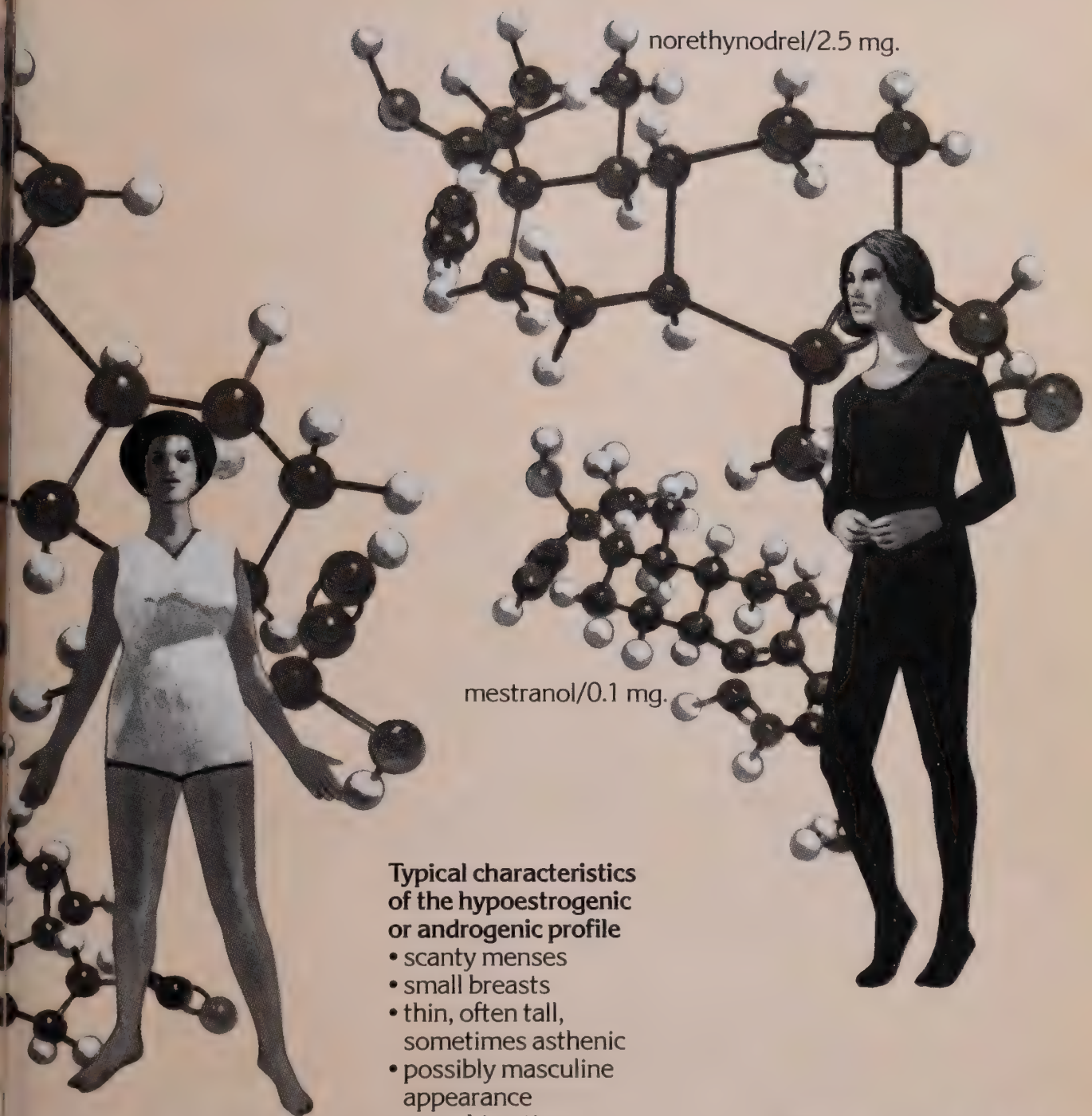
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An increased risk of thromboembolic disease associated with the use of hormonal contraceptives has now been shown in studies conducted in both Great Britain and the United States. Other risks, such as those of elevated blood pressure, liver disease and reduced tolerance to carbohydrates, have not been quantitated with precision.

Long-term administration of both natural and synthetic estrogens in subprimate animal species in multiples of the human dose increases the frequency of some animal carcinomas. These data cannot be transposed directly to man. The possible carcinogenicity due to the estrogens can be neither affirmed nor refuted at this time. Close clinical surveillance of all women taking oral contraceptives must be continued.

Indication—Ovulen and Demulen are indicated for oral contraception.

Contraindications—Patients with thrombophlebitis, thromboembolic disorders, cerebral apoplexy or a past history of these conditions, markedly impaired liver function, known or suspected carcinoma of the breast, known or suspected estrogen-dependent neoplasia and undiagnosed abnormal genital bleeding.

Warnings—The physician should be alert to the earliest manifestations of thrombotic disorders (thrombophlebitis, cerebrovascular disorders, pulmonary embolism and retinal thrombosis). Should any of these occur or be suspected the drug should be discontinued immediately.

Retrospective studies of morbidity and mortality conducted in Great Britain and studies of morbidity in the United States have shown a statistically significant association between thrombophlebitis, pulmonary embolism, and cerebral thrombosis and embolism and the use of oral contraceptives. There have been three principal studies in Britain¹⁻³ leading to this conclusion, and one⁴ in this country. The estimate of the relative risk of thromboembolism in the study by Vessey and Doll³ was about sevenfold, while Sartwell and associates⁴ in the United States found a relative risk of 4.4, meaning that the users are several times as likely to undergo thromboembolic disease without evident cause as nonusers. The American study also indicated that the risk did not persist after discontinuation of administration and that it was not enhanced by long-continued administration. The American study was not designed to evaluate a difference between products. However, the study suggested that there might be an increased risk of thromboembolic disease in users of sequential products. This risk cannot be quantitated, and further studies to confirm this finding are desirable.

Discontinue medication pending examination if there is sudden partial or complete loss of vision, or if there is a sudden onset of proptosis, diplopia or migraine. If examination reveals papilledema or retinal vascular lesions medication should be withdrawn.

Since the safety of Ovulen and Demulen in pregnancy has not been demonstrated, it is recommended that for any patient who has missed two consecutive periods pregnancy should be ruled out before continuing the contraceptive regimen. If the patient has not adhered to the prescribed schedule the possibility of pregnancy should be considered at the time of the first missed period.

A small fraction of the hormonal agents in oral contraceptives has been identified in the milk of mothers receiving these drugs. The long-range effect to the nursing infant cannot be determined at this time.

Precautions—The pretreatment and periodic physical examinations should include special reference to the breasts and pelvic organs, including a Papanicolaou smear since estrogens have been known to produce tumors, some of them malignant, in five species of subprimate animals. Endocrine and possibly liver function tests may be affected by treatment with Ovulen or Demulen. Therefore, if such tests are abnormal in a patient taking Ovulen or Demulen, it is recommended that they be repeated after the drug has been withdrawn for two months. Under the influence of progestogen-estrogen preparations pre-existing uterine fibromyomas may increase in size. Because these agents may cause some degree of fluid retention, conditions which might be influenced by this factor, such as epilepsy, migraine, asthma, cardiac or renal dysfunction, require careful observation. In breakthrough bleeding, and in all cases of irregular bleeding per vaginam, nonfunctional causes should be borne in mind. In undiagnosed bleeding per vaginam adequate diagnostic measures are indicated. Patients with a history of psychic depression should be carefully observed and the drug discontinued if the depression recurs to a serious degree. Any possible

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influence of prolonged Ovulen or Demulen therapy on pituitary, ovarian, adrenal, hepatic or uterine function awaits further study. A decrease in glucose tolerance has been observed in a significant percentage of patients on oral contraceptives. The mechanism of this decrease is obscure. For this reason, diabetic patients should be carefully observed while receiving Ovulen or Demulen therapy. The age of the patient constitutes no absolute limiting factor, although treatment with Ovulen or Demulen may mask the onset of the climacteric. The pathologist should be advised of Ovulen or Demulen therapy when relevant specimens are submitted. Susceptible women may experience an increase in blood pressure following administration of contraceptive steroids.

Adverse reactions observed in patients receiving oral contraceptives—A statistically significant association has been demonstrated between use of oral contraceptives and the following serious adverse reactions: thrombophlebitis, pulmonary embolism and cerebral thrombosis.

Although available evidence is suggestive of an association, such relationship has been neither confirmed nor refuted for the following serious adverse reactions: neuro-ocular lesions, e.g., retinal thrombosis and optic neuritis.

The following adverse reactions are known to occur in patients receiving oral contraceptives: nausea, vomiting, gastrointestinal symptoms (such as abdominal cramps and bloating), breakthrough bleeding, spotting, change in menstrual flow, amenorrhea during and after treatment, edema, chloasma or melasma, breast changes (tenderness, enlargement and secretion), change in weight (increase or decrease), changes in cervical erosion and cervical secretions, suppression of lactation when given immediately post partum, cholestatic jaundice, migraine, rash (allergic), rise in blood pressure in susceptible individuals and mental depression.

Although the following adverse reactions have been reported in users of oral contraceptives, an association has been neither confirmed nor refuted: anovulation post treatment, premenstrual-like syndrome, changes in libido, changes in appetite, cystitis-like syndrome, headache, nervousness, dizziness, fatigue, backache, hirsutism, loss of scalp hair, erythema multiforme, erythema nodosum, hemorrhagic eruption and itching.

The following laboratory results may be altered by the use of oral contraceptives: hepatic function: increased sulfobromophthalein retention and other tests; coagulation tests: increase in prothrombin, Factor VII, VIII, IX and X; thyroid function: increase in PBI and butanol extractable protein bound iodine, and decrease in T³ uptake values; metyrapone test and pregnanediol determination.

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THE USE OF ARTIFICIAL PACEMAKERS IN DIGITALIS TOXICITY

Juan M. Aranda, MD
Charles Johnson, MD, FACP, FACC
Mario R. García Palmieri, MD, FACP

Since the introduction of endocardial pacing in 1959 (1), transvenous pacemakers have become the major therapeutic tool for heart blocks and bradycardias with Stokes-Adams attacks (2). Ventricular pacing has become the treatment of choice for patients with transient heart blocks associated with myocardial infarction (2, 3), and has been used successfully in the treatment of paroxysmal atrial tachycardia alternating with sinus bradycardia and standstill (4, 5). Considerable interest exists in electrical ventricular overdrive by either atrial or ventricular pacing as a means of treating ventricular tachycardia (6, 7). However, this technique has not been widely used for arrhythmias secondary to digitalis toxicity. Although paired electrical ventricular pacing has been shown to be an effective means of overcoming digitalis induced arrhythmias in experimental animals (8), the technique has not been used much in clinical practice because of the danger of inducing ventricular fibrillation while attempting to place the second stimulus at an appropriate time and because the second in-

duced contraction appears to interfere with ventricular filling (9). Recently it has been demonstrated that ventricular pacing with a single electrical stimulus will effectively overcome serious digitalis-induced arrhythmias (10). Beller's (11) results of ventricular pacing in the three most common clinical situations in which ectopic ventricular activity occurs (acute myocardial infarction, digitalis intoxication and after cardiac surgery) prompted us to evaluate our experience with the use of temporary ventricular pacing in digitalis intoxication.

Material and Methods

Six patients with clinical and electrocardiographic evidence of digitalis intoxication were treated for ventricular arrhythmias and/or atrio-ventricular block with temporary ventricular pacing by insertion of a bipolar electrode catheter into the right ventricle. Suppressive drug therapy was contraindicated. Cardio-accelerator drugs did not increase the heart rate, but increased ventricular irritability.

Pacing was performed with a small Medtronic^R external pacemaker. The clinical features as well as the follow-up data are presented in Tables I and II.

Clinical Features

Three patients were male and three females; their ages ranged from 50 to 84 years. Arteriosclerotic heart disease was the clinical diagnosis in five of the patients. All of the patients had been taking diuretic and one patient had received quinidine before ventricular pacing was required. Two of the patients were hypokalemic. Heart failure was a prominent feature in three patients while nausea and vomiting were prominent symptoms in three

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*Study done under NH & L Training Grant No. HL-5342.
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TABLE I: CLINICAL AND ELECTROCARDIOGRAPHIC FEATURES IN SIX PATIENTS WITH DIGITALIS TOXICITY

Case No.	Age/Sex	Clinical Picture	Etiologic Diagnosis	Other Med & Lab Data	Rhythm Before Digitalis Toxicity	Basic Rhythm Before Implantation of Pacemaker	Reasons for Use of Pacemaker
1	50 F	Dyspnea, fatigue, orthopnea, Stokes-Adams	CASHD	Diuril, Hypokalemia	Unknown	Idionodal rhythm frequent ventricular ectopic beats followed by ventricular fibrillation and cardiac arrest. Defibrillated to idionodal rhythm with frequent PVC's.	KCI and suppressive therapy contraindicated pacing rate 80/min.
2	51F	Stokes-Adams	RHD, MS	Quinidine, Diuril, Normokalemia	Atrial fibrillation. Ventricular rate 80-90/min.	Idionodal rhythm 20-30/min. with runs of ventricular tachycardia.	Rate did not increase with atropine. Isuprel increased PVC's. Suppressive therapy contraindicated pacing rate 80/min.
3	71M	Nausea, vomiting, dyspnea, orthopnea & fatigue.	CASHD, HCVD	Diuril, Hypokalemia	Sinus rhythm with trifascicular block.	Atrial fibrillation, high grade A-V block, ventricular bigeminy, alternating with runs of trifascicular block and ventricular bigeminy.	Rate did not increase with atropine. Pharmacologic suppression contraindicated pacing rate 72/min.
4	59F	Nausea, vomiting, dizzy spells, and confusion	CASHD	Diuril, Normokalemia	Normal sinus rhythm.	Second degree A-V block with intermittent complete A-V block.	Rate did not increase with atropine or isuprel. Dizzy spells pacing rate 55/min.
5	65M	Dyspnea, orthopnea, nausea, vomiting, Stokes-Adams.	CASHD	Diuril, Normokalemia	Sinus bradycardia and LAHB.	Atrial fibrillation, high grade A-V block, slow idionodal rhythm, alternating with sinus bradycardia, LAHB, and first degree A-V block.	Rate did not increase with atropine or isuprel, convulsive seizures. Pacing rate 70/min.
6	84M	Palpitations.	CASHD	Diuril, Normokalemia	Atrial fibrillation ventricular rate	Atrial fibrillation, high grade A-V block, multiple PVC's.	Pharmacologic suppression contraindicated.

RHD - Rheumatic Heart Disease. HCVD - Hypertensive Cardiovascular Disease. CASHD - Coronary Arteriosclerotic Heart Disease. A-V - Atrio-ventricular. LAHB - Left Anterior Hemiblock. MS - Mitral Stenosis.

TABLE II: FOLLOW-UP DATA IN SIX PATIENTS WITH DIGITALIS TOXICITY AFTER IMPLANTATION OF PACEMAKER

Case No.	Course
1	Continued with idionodal rhythm, frequent PVC's and runs of ventricular tachycardia suppressed with xylocaine and by increasing the rate of the pacemaker. Returned to NSR after four days. Pacemaker catheter removed on the seventh day. Had cardiac arrest and died on the eighth day. At autopsy multiple pulmonary emboli and mural thrombosis of both ventricles.
2	Returned to NSR after 48 hours, followed 12 hours later by atrial fibrillation with a fast ventricular response. Pacemaker removed after seven days. Digitalis started.
3	Returned to sinus rhythm and trifascicular block after 72 hours, with episodes of second degree AV block (Wencekbach). Pacemaker removed after four days. Redigitalized four weeks later.
4	Second degree AV block persisted after three weeks. Permanent demand pacemaker implanted. Returned to normal AV conduction one week later. Discharged on digitalis.
5	Returned to sinus bradycardia after 72 hours which persisted for 20 days. Digoxin was given because of severe congestive heart failure. Permanent demand pacemaker implanted.
6	Returned to atrial fibrillation with a ventricular rate of 88 per minute after two weeks. Digitalis given every other day.

others at the time of admission. Stokes-Adams attacks developed in three patients before pacemaker implantation; one of them (Case 1) developed ventricular fibrillation and cardiac arrest. She was defibrillated successfully to slow idionodal rhythm.

Two patients (Cases 1 and 4) had developed signs, symptoms and electrocardiographic evidence of digitalis toxicity 1 to 6 months before admission. In Case 1, a transitory junctional rhythm developed one month prior to admission. It disappeared after digoxin was discontinued. In Case 4, bradycardia with premature beats had been detected by another physician 6 months prior to admission.

Electrocardiographic Findings

High grade atrio-ventricular block with a slow idionodal rhythm was the principal manifestation of digitalis toxicity in the cases reported. A junctional reciprocating tachycardia preceded the slow idionodal rhythm in one patient (Figure 1). In addition, four of them showed ventricular irritability as manifested by premature ventricular contractions and runs of ventricular tachycardia. Trifascicular block with ventricular bigeminy and intermittent second degree AV block (Wenckebach) were prominent features in one of the cases presented (Figures 2 and 3). Another patient presented second and third degree atrio-ventricular block (Figure 4).

Ventricular pacing at rates of 70 to 100 per minute

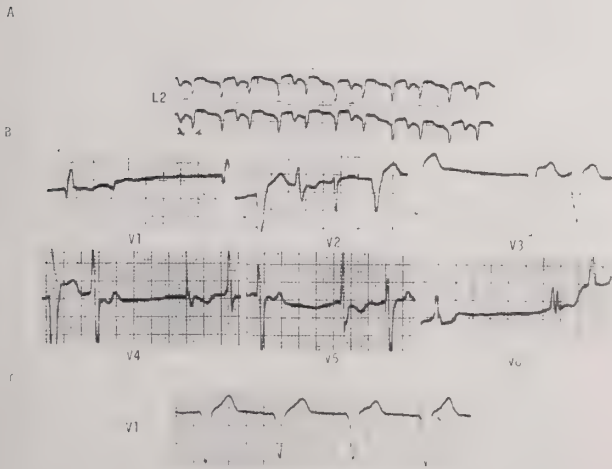


Fig. 1: Case 1. Electrocardiograms. A. Junctional reciprocating tachycardia. B. Several hours after .25 mg digoxin IM, the patient developed an idionodal rhythm with premature ventricular and supraventricular contractions. C. Pacemaker rhythm at a rate of 72 per minute.

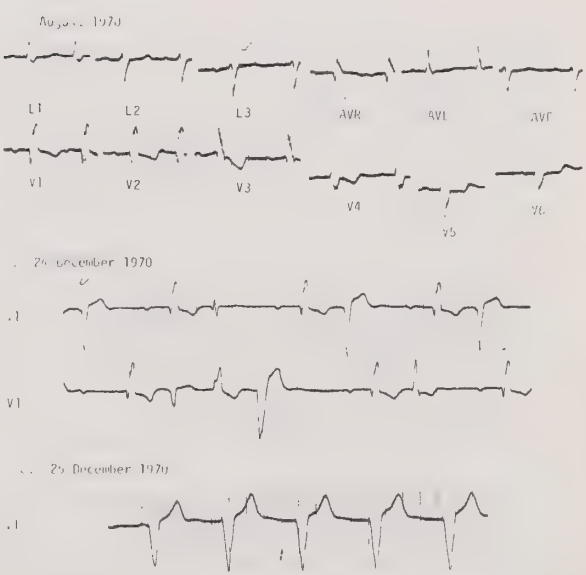


Fig. 2: Case 3. Electrocardiograms. A. RBBB, LAHB, first degree A-V block (suspected trifascicular block). Patient was not on digitalis. B. The strips are not continuous. RBBB, first degree A-V block with ectopic supraventricular and ventricular contractions. Pacemaker inserted.

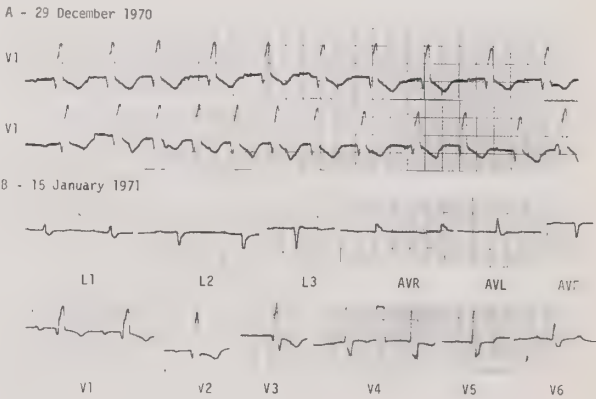


Fig. 3: Case 3. Electrocardiograms. A. Trifascicular block, suspected second degree A-V block (Wenckebach) one day after removal of pacemaker. B. Trifascicular block 18 days after removal of pacemaker.

suppressed the ectopic ventricular beats and runs of ventricular tachycardia in every patient. Of the six patients in our series, one died, probably as a result of an arrhythmia. In this patient (Case 1) the pacemaker was removed on the 7th day, 3 days after she had returned to sinus rhythm with occasional premature ventricular contractions. One day after removal of the pacemaker she suddenly developed ventricular fibrillation and cardiac arrest without warning, from which

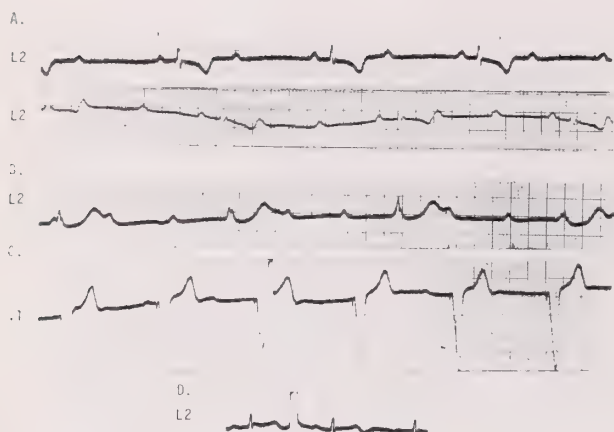


Fig. 4: Case 4. Electrocardiograms. A. The top two strips show second degree A-V block with 2:1 and 3:1 conduction with intermittent runs of complete A-V block (B). C. Demand pacemaker at a rate of 55 per minute. D. Normal sinus rhythm after four weeks.

she could not be resuscitated.

All the other patients returned to the rhythm present before digitalis intoxication, 3 to 21 days after pacemaker implantation and were subsequently discharged from the hospital on digitalis. Two patients, (Cases 4 and 5) required the insertion of a permanent demand pacemaker before they were discharged from the hospital. One patient (Case 5) had developed a Stokes-Adams attack at a time when his rhythm was alternating between sinus bradycardia with left anterior hemiblock and a slow idionodal rhythm. After ventricular pacing and resumption of sinus rhythm, sinus bradycardia persisted for 20 days. During this time he progressively developed congestive heart failure which was not adequately controlled with diuretics and salt restriction. The progressive cardiac decompensation made correction of the bradycardia essential and the demand pacemaker made possible the safe resumption of digitalis. The second patient (Case 4) had had 2 episodes of digitalis intoxication in a period of 6 months. She became disoriented and confused after the appearance of A-V dissociation due to complete A-V block. She developed pulmonary congestion and gallop rhythm which required the use of digitalis in the presence of 2nd degree A-V block, 4 weeks after digoxin was discontinued. The permanent demand pacemaker permitted the safe resumption of digitalis. She returned to normal A-V conduction one week later. In this particular patient the distinction between A-V block produced by digitalis and intrinsic disease per se may be very difficult. A demand permanent pacemaker was indicated in Case 3, but it was not

implanted because of the presence of a malignant lesion in the liver.

The major complications in this series were 2 cases of superficial phlebitis and one case of infection at the cutdown site. In Case 3, displacement of the tip of the catheter was detected after the increase in the endocardial pacing threshold was noticed.

Discussion

There is no specific antidote for digitalis-induced arrhythmias and current methods of treatment are less than satisfactory. However, certain advances in the treatment of digitalis toxicity have been achieved. Most digitalis-induced arrhythmias can be controlled by stopping the drug and correcting hypokalemia. If ventricular irritability is present, potassium can be administered even in the absence of hypokalemia, since these arrhythmias appear to be related to the intracellular loss of potassium from the myocardium (12-14).

Potassium is known to reduce the diastolic depolarization of ectopic pacemakers and to slow conduction through specialized conduction tissue. In the presence of digitalis this depression of conduction is potentiated (15). Because of this synergism it should be administered with caution or should not be administered at all in digitalis-induced advanced atrio-ventricular block. Quinidine and procainamide are useful in reducing increases automaticity produced by digitalis; however, these drugs may lead to the induction or worsening of A-V block (16) by decreasing the membrane resting potential with a subsequent reduction in the maximal rate of depolarization. This could have been a significant factor in one of our patients (Case 2). Therefore, their use is limited to arrhythmias unassociated with serious degrees of atrio-ventricular block. Lidocaine apparently is more effective than procainamide or quinidine in the treatment of digitalis-induced ventricular tachycardia, ventricular ectopic beats (17) and causes less depression of cardiac contractility than quinidine and procainamide (18). It can be used in the presence of A-V block since it is reported not to affect the conduction velocity in the A-V node and the ventricular myocardium (19). This agent together with ventricular pacing was very effective in suppressing ventricular irritability in one of the cases reported (Case 1).

Propanolol has been found to be particularly effective in the treatment of certain digitalis-induced tachyarrhythmias (16). Like quinidine and procainamide, it diminishes conduction velocity and its use appears to be limited to tachyarrhythmias and ventricular extrasysto-

les without serious degrees of A-V block (20, 21). Diphenylhydantoin is a useful drug in digitalis-induced arrhythmia with depressed A-V conduction and increased ventricular automaticity. It depresses glycoside-induced ventricular automaticity while it increases atrio-ventricular nodal conduction with little or no depression of intraventricular conduction or sinus rate (22). The drug has also been shown to dissociate the inotropic and arrhythmic action of digitalis, thus depressing digitalis-induced tachyarrhythmias without diminishing the contractile effects of the glycoside (23). However, several reports have focused attention on the myocardial depressive effects of intravenously administered diphenylhydantoin (24, 25), and in some patients, large doses of diphenylhydantoin have produced transient atrio-ventricular block and sinus arrest (26).

Another agent which theoretically may be used in glycoside-induced arrhythmias secondary to depressed conduction is bretylium tosylate. It causes an increase in the membrane resting potential (hyperpolarization), as a result the maximal rate of depolarization is also increased, and consequently the conduction velocity will be higher (27-29).

Glucagon has also been shown to enhance A-V conduction, sinus and atrio-ventricular node pacemaker activity (30). In experimental animals, glucagon did not increase digitalis-induced arrhythmias but ameliorated them by virtue of its chronotropic action, which produced a pacemaker overdrive (31).

In spite of these advancements in the treatment of digitalis toxicity the patient who manifests digitalis-induced arrhythmias with depression of atrio-ventricular conduction and an ectopic pacemaker presents a difficult therapeutic problem.

In this condition the usual antiarrhythmic agents are contraindicated. If the ventricular pacemaker is junctional or high in the His bundle, atropine may be effective in terminating A-V block (13). However, the therapeutic success is unpredictable, as noticed in some of our patients. In cases where augmentation of the vagal tone by digitalis is a significant factor, the effect of atropine may be salutatory. As shown in Case 2, isoproterenol increased ventricular ectopic activity. In the presence of toxic levels of digitalis, it may increase ventricular automaticity (13). The solution to this therapeutic problem may be provided by artificial ventricular pacing. By artificial stimulation of the ventricles at a rate higher than that of the slow idionodal focus suppression of the secondary ectopic focus may be accomplished, thus avoiding the necessity of using antiarrhythmic agents in the presence of atrio-ventricular block.

The technique has not been used frequently in clinical practice because of the electrical hazard of provoking spontaneous arrhythmias, since digitalis lowers the threshold for spontaneous repetitive ventricular extrasystoles in response to pacemaker stimuli (32). Another possible hazard is that of further potassium loss from the myocardium as a result of the electrical stimuli delivered at high frequencies (33). Leon-Sotomayor *et al* (34) were probably the first to report the successful use of an intracardiac pacemaker in the treatment of digitalis-induced arrhythmia. Their patient developed complete atrioventricular block with recurrent periods of ventricular asystole refractory to conventional drug therapy and to the use of external pacing. Cardiac activity was maintained by the internal pacemaker for 14 days after which the patient had a nodal rhythm with A-V dissociation. She regained normal sinus rhythm within 72 hours. In 1964, Sowton, Leatham and Carson (35) used temporary artificial ventricular pacing to treat two patients who developed rapid ventricular arrhythmias refractory to conventional drug therapy. One of them had been receiving digitalis, diuretics, morphine and anticoagulants. Although not mentioned in their report, digitalis intoxication possibly precipitated by potassium loss from the use of diuretics, could have been a factor in the genesis of the arrhythmia. Later, Heiman, Helwig (36) and Lew (37) reported the successful use of transvenous intracardiac pacing in the treatment of ventricular arrhythmias due to digitalis. One of their patients, a 42-year old housewife, received digoxin, 2 mgs by mouth over a 12-hour period. She developed ventricular bigeminy alternating with runs of ventricular tachycardia and fibrillation not controlled with potassium or procainamide. Temporary ventricular pacing abolished ventricular irritability and gained control of the ventricles.

In the report of Hornbaker *et al* (38) a patient developed digitalis intoxication manifested by second degree A-V block and ventricular irritability. A temporary electrode catheter was placed in the apex of the right ventricle. The ventricular irritability was abolished by pacing the ventricle at a rate of 130/minute. Chung (39) in his review of digitalis intoxication, reported two patients with complete atrio-ventricular block in whom temporary ventricular pacing was used with excellent results and Kastor *et al* (40) did not report any complications in their experience with transvenous atrial pacing in the treatment of digitalis-induced ventricular arrhythmias.

In 1965, Frommer *et al* (8) demonstrated in animal studies that paired electrical stimulation of the ventricles

can effectively eliminate digitalis-induced arrhythmias, however, this technique has not been used clinically because of the danger of inducing ventricular fibrillation and because the second induced contraction appears to interfere with ventricular filling. It was not until 1970 that Zelis *et al* (10) showed that ventricular pacing with a single electrical stimuli accomplished the same effect in digitalis-induced arrhythmias. In their experiments, ventricular pacing appeared to be more effective than the administration of potassium in terminating the arrhythmia. However, neither ventricular pacing nor potassium altered the maximal tolerated dose of digitalis. At about the same time of this report, Patton (41) *et al* reported in 1970 3 patients with refractory congestive heart failure in whom the use of digitalis was associated with serious bradyarrhythmias. In each, the implantation of a permanent demand transvenous pacemaker, permitted the safe resumption of digitalis with marked clinical improvement. Beller (11) reported 5 patients with digitalis toxicity in whom ventricular pacing was of value for control of ectopic ventricular beats and recurrent ventricular tachycardia. In his series, one patient required the later insertion of a permanent pacemaker for control of supraventricular tachycardia and marked sensitivity to digitalis and quinidine. This same problem was encountered in two of our patients. A demand permanent pacemaker permitted the safe resumption of cardiac glycosides. In the same report (11) another patient who had runs of premature ventricular contractions and ventricular tachycardia, unresponsive to lidocaine, required ventricular pacing. Three days after the electrode catheter was removed from the right ventricle, sudden cardiac asystole occurred. It is possible that in this case as well as in our patient (Case 1) the presence of the catheter in the right ventricle would have permitted successful resuscitation.

The mechanism by which ventricular pacing offsets ventricular automaticity and gains control of the ventricular rate appears to be that the electrical stimulus is delivered at a more rapid rate than the frequency of the idionodal or idioventricular focus thereby suppressing the ectopic pacemaker (42). The frequency of the electrical rate may be reduced to a rate even slower than that of the original idiopathic pacemaker, as the electrical pacemaker is capable of depressing the slope of diastolic depolarization (automaticity) of the ectopic focus (42). In addition to the rate increase effected in all patients, Beller (11) suggested that the pacemaker-induced conduction defect (left bundle branch block) may help to extinguish potential pathways

for reentry within the ventricles by initiating ventricular depolarization from a different site and through a different pathway. Spontaneous repetitive ventricular extrasystoles in response to pacemaker stimuli or significant loss of potassium from the myocardium have not been observed in the cases reported. Apparently the effect of rapid ventricular stimulation to depress spontaneous pacemaker activity predominates over the digitalis-induced increased sensitivity to electrical stimulation (10).

In light of the previous experiences it seems that the indications for ventricular pacing in digitalis toxicity may be summarized as follows:

1. ectopic rhythms due to reentry or enhanced automaticity that require therapy but are not controlled with the standard drugs.
2. allergy of the patient to the standard drug.
3. the drug used for treatment depresses myocardial contractility.
4. depression of pacemaker (SA arrest).
5. depression of conduction (A-V block, reciprocation) unresponsive to standard drugs or in which the drug causes ventricular irritability.
6. depression of conduction (A-V block) with ectopic pacemakers.

Use of pacemakers with a fixed rate are not recommended because of the danger or provoking a pacemaker-induced parasystolic rhythm that would compete with the patient's basic rhythm or ectopic rhythm and result in ventricular tachycardia or fibrillation (43). The use of ventricular pacing in some of the indications outlined above would permit the safe administration of drugs that could possibly depress further A-V conduction. It should be re-emphasized that ventricular pacing should not be utilized as the initial approach in the treatment of digitalis-induced arrhythmias, but should be employed only when standard measures fail. It is a relatively simple procedure without serious complications if the necessary precautions are taken and good clinical judgment prevails.

Summary

Six patients with clinical and electrocardiographic evidence of digitalis toxicity were treated for ventricular arrhythmias and/or atrioventricular block with temporary ventricular pacing. High grade atrioventricular block with a slow idionodal rhythm was the principal manifestation of digitalis toxicity in five of the patients. In addition, four of them showed ventricular irritability as manifested by premature ven-

tricular contractions and runs of ventricular tachycardia. The sixth patient presented second and third degree atrioventricular block. Inability to increase the rate with pharmacological agents without increasing ventricular automaticity and contraindications for suppressive drug therapy were the main indications for ventricular pacing. Ventricular pacing suppressed the ectopic ventricular focus in five of the cases presented. One patient died suddenly one day after removal of the pacemaker. Five patients were discharged from the hospital. A permanent demand pacemaker was implanted in two patients, thus permitting safe resumption of digoxin.

The mechanism by which ventricular pacing offsets ventricular automaticity and gains control of the ventricular rate appears to be that the electrical stimulus is delivered at a more rapid rate than the frequency of the idiopathic ventricular focus thereby suppressing the ectopic pacemaker. Others have suggested that the pacemaker-induced conduction defect may help to extinguish potential pathways for reentry within the ventricles by initiating ventricular depolarization from a different site and through a different pathway. Ventricular pacing at a rate higher than the basic idionodal focus, suppresses ventricular irritability, thus avoiding the use of antiarrhythmic agents in the presence of atrioventricular block.

Resumen

Seis pacientes con evidencia clínica y electrocardiográfica de intoxicación con digital fueron tratados con un marcapaso externo temporero debido a ritmos ectópicos ventriculares y/o bloqueo atrioventricular. Bloqueo atrio-ventricular con un ritmo idionodal lento fue documentado en 5 pacientes. En cuatro de ellos se notó contracciones ventriculares prematuras y taquicardias ventriculares. El sexto paciente presentó bloqueo atrioventricular en segundo y tercer grado. Las indicaciones para el uso del marcapaso fueron la incapacidad de aumentar la frecuencia cardíaca con agentes farmacológicos sin aumentar la automaticidad ventricular y contraindicaciones para el uso de agentes supresivos. Un paciente murió súbitamente 1 día después de haber sido removido el marcapaso. Cinco pacientes fueron dados de alta. Un marcapaso permanente de demanda fue implantado en 2 pacientes lo cual permitió la continuación de digital.

El mecanismo por el cual los marcapasos ventriculares inhiben la automaticidad ventricular parece ser debido a que la frecuencia del estímulo eléctrico es más

rápida que la frecuencia del foco ventricular ectópico. Se ha propuesto de igual forma que el defecto de conducción inducido por el marcapaso ayuda a extinguir senderos potenciales de re-entrada en el ventrículo.

El uso de marcapasos ventriculares a una frecuencia más alta que la frecuencia del ritmo idionodal suprime la irritabilidad ventricular evitando de esta forma el uso de agentes supresivos en presencia de bloqueo atrio-ventricular.

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MANEJO ACTUAL DE INFECCIONES URINARIAS

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Dr. Cangiano:

Durante las décadas pasadas se adelantó mucho en el estudio y tratamiento de las infecciones urinarias pero todavía existe controversia en el manejo de las mismas.

Vamos a discutir algunos de estos puntos controversiales. Empezaremos por el tema de pielonefritis.

Una paciente mujer de 25 años de edad se admite con un dolor de flanco agudo, escalofrío, fiebre, frecuencia y ardor al orinar; el análisis de orina enseña muchas células blancas, ¿cómo usted manejaría este caso?

Dr. Ramírez-González:

El cuadro sugiere una pielonefritis aguda o una

infección urinaria aguda con extensión a parenquima renal. Específicamente la paciente está sintomática y tóxica. Necesita hospitalización y tratamiento por un período de 10 a 14 días con terapia intravenosa, con un antibiótico bactericida y de amplio espectro, como por ejemplo la Ampicilina (Polycillin). Hay que establecer un diagnóstico específico, y la piuria que presenta este paciente no necesariamente correlaciona con la bacteriuria; puede ocurrir piuria en ausencia de bacteriuria o viceversa. El diagnóstico definitivo de una infección urinaria es bacteriológico y la prueba más importante es un cultivo de orina para procesar cuantitativamente. Se conocen los problemas en la toma del cultivo de orina. Nosotros abogamos por el llamado "mid stream clean catch urine" que debe tomarse en condiciones ideales estériles ya por una enfermera o supervisada por el médico, no en una cama sino en una mesa de examen para exponer bien los genitales, y separar los labios. Después de irrigar y lavar bien el perineo con PhisoHex la muestra se toma en un envase estéril preferiblemente de boca ancha. La uretra distal y el área del perineo contienen un sinnúmero de bacterias, usualmente las mismas que aparecen en la flora intestinal que contaminan este tipo de muestra. La orina es un medio de cultivo excelente, y permite multiplicación bacteriana rápida, que puede ocasionar un resultado falsamente positivo. Si no fuera posible procesarla inmediatamente puede ser refrigerada entre 5 o 10 días sin alterar significativamente el conteo bacteriano de la misma. Luego de tomar el cultivo de orina debe hacerse un extendido de la orina sin centrifugar y una tinción de Gram. Si se demuestran bacterias y el conteo bacteriano en el cultivo es significativo, o sea que contiene más de 100,000 colonias, se amerita comenzar tratamiento.

La terapia intravenosa con antibiótico bactericida de amplio espectro debe rendir la orina estéril en 48 a 72 horas, a este tiempo nos gusta repetir el cultivo y saber así cuán adecuada es la terapia. Se trata al paciente por 10 o 14 días según la severidad del caso y del organismo. Cualquier cambio responde al antibiograma. Quizás lo más importante es enfatizar

Panel presentado en la Convención Anual del Distrito Este de la Asociación Médica de Puerto Rico en el Hospital Municipal de San Juan el 7 de junio de 1972, auspiciado por el Hospital de Veteranos de San Juan, Puerto Rico.

al paciente que no importa cuál es el tratamiento, la mayor parte de las infecciones urinarias sintomáticas tratadas se tornan asintomáticas en cuestión de 3 o 4 días, pero la bacteriuria puede persistir. Por lo tanto se exige en el manejo de estos casos el seguimiento a largo plazo. Debe repetirse el cultivo de orina varios días después de completar el tratamiento y luego a intervalos repetidos por los próximos 4 o 6 meses.

Dr. Cangiano:

Noté que el Dr. Ramírez-González no mencionó el sondeo como medio de obtener un cultivo de orina. Para diagnosticar pielonefritis, el criterio más confiable ha sido obtener orina o bacterias del riñón afectado cuando se cateteriza el ureter. También sabemos que en un espécimen orinado los límites de confiabilidad de obtener un cultivo positivo son de 80 por ciento. Esto sube al 95 por ciento en el segundo cultivo y cuando se cateteriza el paciente es 95 por ciento. Ahora, ¿hay alguna indicación para cateterización como medio de obtener un cultivo?

Dr. Isaías:

Sí, de hecho la cateterización ha sido un punto de discusión particularmente entre los urólogos y los internistas. En su mayoría los internistas rechazan el sondeo por considerarlo traumático, que no ofrece toda la garantía necesaria y de aquí surgió el sistema del "clean catch mid stream specimen". Todos los medios de obtener el cultivo de orina o muestra tiene sus pros y sus contras. El sondeo, usado juiciosamente, ofrece desde el punto de vista urológico quizás el medio más efectivo de uno obtener una muestra confiable. Desde luego, no todos los cultivos obtenidos por sondeo son tomados adecuadamente. Ya el Dr. Ramírez-González abundó en los problemas de tomar una muestra. El paciente debe prepararse quirúrgicamente y no todo el mundo se toma el tiempo, ni el trabajo, ni tiene la habilidad de hacerlo sin contaminar el espécimen. El trauma se puede eliminar usando una sonda pequeña.

Dr. Cangiano:

En un paciente que tiene enfermedad recurrente o infección recurrente, ¿ustedes lo sondan repetidamente?

Dr. Isaías:

Sí, porque esta no es una prueba a hacerse sin indicación. Para obtener una prueba de cultivo se sondea digamos hoy y la otra muestra no se toma hasta después de dos semanas de tratamiento adecuado, o sea, que el

procedimiento no es tan frecuente y si lo hace una persona capacitada y con todas las precauciones necesarias no hay contraindicación a repetir el sondeo.

Dr. Cangiano:

Dr. Pascual, ¿cómo ve usted este problema en los niños?

Dr. Pascual:

Primeramente, nosotros obtenemos una muestra de orina "mid stream clean catch" en casi todas las ocasiones. En algunos usamos aspiración suprapúbica, pero solamente cuando está indicado, por ejemplo, en los niños recién nacidos donde hay problemas en evitar contaminación del espécimen, o cuando cultivos repetidos demuestran entre 10,000 y 100,000 colonias repetidamente, entonces queremos cerciorarnos de si en realidad tiene bacteriuria o no. Generalmente, la aspiración suprapúbica se hace en infantes menores de 2 años porque en esta edad la vejiga es un órgano abdominal y es más fácil obtener un espécimen de orina. En cuanto a la preparación, es muy importante que el paciente esté bien hidratado y que no haya orinado por lo menos en las dos horas anteriores.

Dr. Cangiano:

¿Cómo se hace una punción suprapúbica?

Dr. Pascual:

Después de preparado el paciente con Phisohex, y con Betadina, se orienta la aguja perpendicular a un ángulo de 10 a 20 grados hacia abajo y a uno o dos centímetros sobre el sínfisis, se pasa a la vejiga y hay que aspirar para obtener la muestra. Es importante hacer presión en la uretra al mismo tiempo, al varón sobre la uretra penil y en las niñas por el recto. Se usa generalmente una aguja número 20 de pulgada y media con una jeringuilla de 10 cc. La complicación mayor es hematuria e impide utilizar rutinariamente este procedimiento para obtener muestras de orina porque esta complicación puede confundir. También se ha informado ocasionalmente la perforación intestinal pero esto no ha sido complicación mayor.

Dr. Cangiano:

Uno de los problemas importantes es determinar cuándo hay una infección activa y significativa. ¿Qué criterios tenemos para determinar esto?

Dr. Bermúdez:

Deben considerarse los síntomas del paciente, sobre

todo, fiebre, dolor en el flanco o síntomas urinarios que indiquen la posibilidad de una infección activa. Si el conteo de colonias pasa de 100,000 por ml se consideraría una infección activa con el cuadro clínico. Entre 10,000 y 100,000 colonias debe repetirse el cultivo. Un paciente con síntomas relativamente clásicos de pielonefritis o de infección urinaria que mantenga un cultivo de menos de 100,000 colonias con el mismo organismo y con la misma sensibilidad, deberá tener tratamiento.

Dr. Cangiano:

En un paciente con 10,000 colonias/ml de pseudomonas y antecedentes de una infección, ¿puede considerarse significativo ese cultivo de 10,000 colonias?

Dr. Bermúdez:

Si es la segunda infección del paciente, yo mismo le repetiría el cultivo, si se obtienen las mismas 10,000 colonias, se podría estudiar la osmolalidad a ese paciente y determinar si está baja.

Dr. Cangiano:

¿Qué importancia conlleva eso?

Dr. Bermúdez:

Cuando ocurren las infecciones urinarias, se afecta la médula del riñón y se altera la concentración de la orina, perdiéndose la habilidad para concentrar la orina. Esto permite que se prolongue la infección y posiblemente las defensas del riñón no puedan erradicar la infección. Por lo tanto la osmolalidad de la orina en estos casos nos podría ayudar a decidir tratar esa infección.

Dr. Cangiano:

¿Cuáles son los organismos más frecuentes en pielonefritis aguda?

Dr. Bermúdez:

Son los Gram negativos. *Escherichia coli* es mayormente el organismo que se recupera, seguido por *Proteus* y *Klebsiella-Enterobacter*. De vez en cuando la infección inicial es *Pseudomonas* pero no es tan común. Los otros organismos encontrados son el *Enterococo* y *Streptococo* beta hemolítico. Pueden considerarse un contaminante si no se está enterado que enterococo frecuentemente infecta la orina. De los otros organismos sabemos que estafilococo infecta la orina en los pacientes diabéticos y en presencia de estafilococo debe sospecharse un absceso intrarenal. También en pacientes que han

recibido antimetabolitos conjuntamente con dosis altas de antibióticos puede haber una superinfección por hongos tales como *Cándida* y puede desarrollarse una pielonefritis por *Cándida*.

Dr. Cangiano:

¿Qué pacientes hospitaliza y qué pacientes trata ambulatoriamente cuando desarrollan una infección urinaria?

Dr. Bermúdez:

Este problema es básicamente de disponibilidad de camas. Recordemos que la mayoría de estas pacientes son jóvenes y que hospitalizarlas puede crear problemas familiares. También, hay riesgo en enviar a la casa a una paciente con infección urinaria, y si se hace, debe mantenerse contacto con la paciente por las primeras 24 a 48 horas y tratarla con un agente bactericida. Yo estoy seguro que el 80 por ciento de las pielonefritis que ocurren son tratadas en la casa de modo ambulatorio.

Dr. Cangiano:

¿Su terapia inicial sería un agente bactericida?

Dr. Bermúdez:

Sí, preferiblemente Ampicilina o Cefalosporina.

Dr. Cangiano:

¿Y la sulfa?

Dr. Bermúdez:

Sulfá es bacteriostático y para erradicar la bacteria en pielonefritis con infección del parenquima renal debemos usar un agente bactericida. Tenemos el problema de que la mayoría de los agentes bactericidas al presente son penicilinas y sus derivados y en estos casos es preferible usar la cefalosporina aunque quizás nos tomamos un riesgo parcial ya que algunos de estos pacientes son igualmente alérgicos.

Dr. Cangiano:

Vamos a otro caso. Una niña de 3 años con un desarrollo agudo de escalofrío, fiebre, dolor en el flanco, ardor al orinar y piuria. ¿Cómo se manejaría?

Dr. Pascual:

El manejo de esta paciente no va a diferir mucho de lo discutido ya. Tendríamos que establecer el diagnóstico. Sobre esto quiero recalcar que muchas veces uno necesita una muestra de orina y el niño

no quiere orinar y generalmente se le indica que tome líquido para que orine. Si obtenemos una muestra de orina va a estar diluída. Al hacer un conteo y obtener un valor intermedio entre 10,000 y 100,000 colonias por ml no podemos establecer un diagnóstico y si es un paciente que esté bastante enfermo y se ha comenzado el tratamiento luego de obtener el cultivo, no vamos a tener la oportunidad de poderle repetir el cultivo. Quiero recalcar también la importancia de repetir un cultivo 48 horas después de comenzados los antibióticos. En general muchos de estos pacientes se vuelven completamente asintomáticos lo cual quiere decir que la infección se haya erradicado. Si ellos continúan teniendo bacteriuria está indicado hacerle un nuevo cultivo.

En estos niños también se aconseja un pielograma intravenoso y un cistograma después de haber tenido la primera infección.

Dr. Cangiano:

En la historia natural de pielonefritis hay un período en la infancia en que se puede ver pielitis y es sintomático, puede aparecer un período inaparentemente activo o inactivo o puede haber cura. Más tarde aparece lo que se llama la cistitis de luna de miel y también puede aparecer la cistitis de la píldora contraceptiva y hay algunos médicos que hasta le han recomendado a sus pacientes que se casen para evitar este problema, pues la promiscuidad sexual y el trauma uretral puede ser mucho mayor. Otro de los períodos críticos es durante el embarazo y más tarde la pielonefritis de los 40 años en que puede desarrollarse uremia. Para hablarnos de esto vamos a presentarle al Dr. Axtmayer el siguiente problema:

Una señora de 26 años de edad, con dos hijos, tiene amenorrea de 4 meses y se presenta con escalofrío, fiebre, dolor en el flanco y ardor al orinar, ¿hay algún aspecto de este paciente diferente a los otros casos?

Dr. Axtmayer:

Primero, por supuesto, tenemos que hacerle un buen historial y un físico y confirmar si está embarazada. En el embarazo el problema de infecciones urinarias puede estar asociado con algunos cuadros más serios como bacteremia o shock bacterémico. Puede afectar al feto y causar muerte intrauterina, parto prematuro y una morbilidad y mortalidad perinatal mucho más alta. Debido a la atonia que producen las hormonas progestágenas y a los factores mecánicos del embarazo hay estancamiento de la orina y estas infecciones se manifiestan más frecuentemente. Alrededor del 2 al

6 por ciento de las mujeres embarazadas tienen bacteriuria sin síntomas, a esas le hacemos cultivos y le administramos tratamiento preventivo. Pero la base del tratamiento en el embarazo es antibióticos y líquidos abundantes. Estas pacientes deben hospitalizarse. Hay ciertos puntos que difieren, evitamos administrar ciertas medicinas en el embarazo. Por ejemplo, el Gantrisin puede causar hiperbilirubinemia en el recién nacido. Sabemos que la tetraciclina mancha los dientes de los recién nacidos, y que la terramicina está asociada a ciertas drogas que no nos gusta usar, por eso casi siempre empezamos el tratamiento inicial con Ampicilina o Furadantina.

Dr. Cangiano:

¿Cómo prevenirse la infección urinaria en la mujer embarazada?

Dr. Axtmayer:

Volvamos al problema de la bacteriuria. Si una mujer está embarazada se debe hacer un examen para bacteriuria y atacar el organismo que la causa. Después del puerperio debe estudiarse estas pacientes para descartar lesiones urológicas, como una estrechez en la uretra, reflujo o obstrucción uretérica.

Dr. Cangiano:

La audiencia planteará preguntas al panel.

Dr. Juan Jiménez:

Muchas veces la vulvo vaginitis en niñas puede causar un problema diagnóstico, ya que tendríamos anomalías en la orina y en el cultivo. ¿Cómo podría diferenciarse entre esta entidad y una infección urinaria?

Dr. Pascual:

Niñas con flujo vaginal demostrarán piuria pero un buen cultivo de orina será negativo. No es difícil diferenciar una cosa de la otra.

Dr. Isaacs:

En los países tropicales como Puerto Rico, sabemos que las mujeres frecuentemente padecen de secreciones vaginales y la tricomoniasis y la moniliasis son bien frecuentes. Por esta razón debe tomarse una muestra con sonda.

Dr. Osvaldo González:

¿Cuán confiable es un cultivo bien tomado que contenga más de un organismo?

Dr. Bermúdez:

Yo creo que pueden haber infecciones mixtas de la orina. Hemos visto cultivos de 3 o 4 organismos y creo que esos están contaminados y se debían de repetir. Pueden haber infecciones mixtas como en una bacteremia con dos organismos pero se debía de repetir para asegurarnos de ello.

Dr. Jesús Vázquez:

En la opinión del panel, ¿qué es un cultivo positivo?

Dr. Bermúdez:

Yo considero 100,000 o más una prueba sólida de que el paciente tiene una infección urinaria.

Sra. María Medina (Bacterióloga)

La experiencia en bacteriología, es que esos niveles de conteo son aplicables siempre y cuando el paciente no esté recibiendo antibióticos, porque el conteo entonces puede ser bajo, por ejemplo 10,000 y sin embargo el paciente tiene sintomatología clínica. Es 100,000 siempre y cuando el paciente no esté recibiendo antibióticos.

Dr. Rodríguez-Torrens:

Si después de un curso de 14 días con antibióticos se le repiten los cultivos de orina y se obtiene el mismo organismo, cabrían dos posibilidades: que fuera el organismo inicial del mismo tipo o que fuera uno de diferente tipo.

Dr. Ramírez-González:

Las posibilidades son tres: hubo reinfección o no se erradicó el organismo inicial porque la terapia fue inadecuada o desarrolló resistencia a la droga que se le estaba administrando. Determinar cuál de las 3 posibilidades está presente sería académico. Lo importante es que se debe considerar un relapso de la infección y ya el tratamiento se modifica un poco. Se duplica el tiempo de tratamiento, si le dimos 10 días de terapia inicial, se le van a dar 20 días, si se le dieron 14 se le dan 28. Y ya empezamos a buscar causas que predispongan a este paciente a una infección urinaria; si es diabético o si tiene anomalías congénitas de vías urinarias que predisponen y perpetúan una pielonefritis. Se necesitan estudios radiológicos como el pielograma intravenoso, cistoscopia, y cistouretrograma para ver si hay estrechez en el tracto urinario bajo. Una vez se completa ese curso de antibióticos debe ponerse al paciente en terapia de supresión a largo plazo, no con un antibiótico de amplio espectro, sino con un agente antimicrobiano que podría

ser la sulfonamida de duración corta, el ácido nalidixico, mandelamina o la furadantina. Esta terapia debe administrarse 4 a 5 veces dependiendo de la severidad del organismo, con cultivos periódicos cada dos o tres meses.

Dr. Cangiano:

Los casos de recurrencia que el Dr. Ramírez-González nos hablaba podrían conllevar un problema financiero al paciente ya que cada cultivo tiene un valor de \$25.00. ¿Existen métodos de medir la presencia de una infección urinaria menos costosos e igualmente confiables al cultivo de orina?

Dr. Pascual:

Existe el grupo de las pruebas enzimáticas en las cuales está la prueba de nitrito de Griess, también está la prueba de catalasa urinaria, la prueba de trifeniltetrazolim y la prueba de beta-glucuronidasa. Todas estas pruebas enzimáticas no son muy efectivas para decidir si haya infección o no. Una prueba que ayuda muchísimo y es bastante rápida, es la que se discutió anteriormente: examinar una muestra sin centrifugar de orina teñido con solución de Gram. También hay otros métodos, el método de testuria y el bacti-check que son cultivos rutinarios pero que se hacen en la oficina del médico. Se pueden leer a las 24 horas y el costo es bajo, sale en alrededor de \$.65 cada prueba.

Dr. Cangiano:

¿Y cuán confiable es?

Dr. Pascual:

Confiable es sobre 90 por ciento. Compara con los cultivos corrientes si uno tiene un cultivo positivo puede enviar eso para hacerle sensibilidad y verificar.

Dr. Cangiano:

¿Qué consideraciones tendría usted sobre el antibiótico en insuficiencia renal?

Dr. Bermúdez:

Un aspecto muy común en pacientes tratados con antibióticos por períodos largos de tratamiento específicamente con aminoglicósidos es que pueden desarrollar insuficiencia renal. Otro aspecto es que al administrar antibióticos se debe considerar la función renal de los pacientes. Hay tablas publicadas en el uso de antibióticos en insuficiencia renal. Una regla simple y básica es que si el paciente tiene una depuración de creatinina de menos de 30 cc por minuto debe tratarse como un paciente con insuficiencia renal severa.

A este paciente se le debe administrar una dosis máxima, en las primeras 24 horas y luego una tercera parte de esa dosificación cada 48 horas. Usando kanamicina se puede seguir la regla del 9. Esta regla implica que la creatinina sérica se debe multiplicar por el número 9 y eso le da el intervalo de horas con que debe dar la medicación. Con Gentamicina se sigue la regla del 8, en la cual se multiplica la creatinina por 8 y eso le da el intervalo con que debe darle la dosis. Se está usando en dosis de 3 a 5 mg. por kilo por día en infecciones severas y uno calcula esa dosificación y la administra a ese intervalo. Yo creo que la mejor manera de hacerlo es la medida de los niveles en sangre del antibiótico y posiblemente la medida de los niveles en orina. Furadantina no se le debe dar a un paciente con insuficiencia renal, por la sencilla razón que la excreción de Furadantina depende de una buena función renal y se acumula pudiendo desarrollar una neuropatía severa.

Dr. Cangiano:

Se ha recomendado tomar mucha agua como parte del tratamiento de infección y hay una base científica para esto. Quizás el Dr. Ramírez-González nos pueda hablar sobre el uso de diuresis en el tratamiento de infecciones urinarias.

Dr. Ramírez-González:

Como mencionó anteriormente el Dr. Axtmayer en su exposición nosotros usamos la diuresis forzada en el tratamiento de infecciones urinarias agudas y creo que hay bastante base experimental y científica para justificarlo. Por medio del mecanismo de concentración del orina del riñón la médula es hipertónica. Sabemos que organismos que son atacados por el antibiótico y se transforman en formas "L" o en protoplastos sin pared celular son protegidos por el medio hipertónico de la médula y persisten aún después de discontinuar los antibióticos y pueden revertir a las formas originales, crear una pared celular y volver a reinfectar al paciente. Si le damos líquidos por boca a este paciente y hacemos que el riñón diluya y pierda la capacidad de concentración a nivel papilar, vamos a bajar la osmolalidad y estos protoplastos van a desaparecer. Otro punto interesante es que la concentración de amonía a nivel distal en el nefrón correlaciona con una inhibición del cuarto componente de complemento y si se inhibe el cuarto componente de complemento, la acción contra tejido extraño, como sería una bacteria, está impedida. Si bajamos la concentración de amonía por el medio de una diuresis forzada podríamos hacer que este cuarto componente de complemento no se inactivara. En adición la activi-

dad fagocítica del leucocito es también alterada por la concentración de amonía. Si diluimos la amonía, induciendo una diuresis y bajando la osmolalidad, ayudamos al huésped, en este caso el paciente, a combatir la infección.

Dr. Cangiano:

Dr. Axtmayer, usted también ha visto mucha cistitis especialmente en la mujer embarazada, ¿podría hablar-nos sobre los factores que predisponen a estos y mencionarnos algo sobre el uso de duchas vaginales?

Dr. Axtmayer:

La cistitis es casi siempre secundaria a algún otro factor y lo que llamamos cistitis en realidad no es cistitis sino es una uretritis, los síntomas que tiene son más de la uretra que de la vejiga. En cuanto a duchas vaginales considero son completamente innecesarias 99.99 por ciento de las veces, eso es algo que se trae desde siglos anteriores y en el embarazo no se deben usar. Fuera del embarazo, ocasionalmente pueden usarse en una paciente que considera tiene algún olor ofensivo, pero en verdad las duchas vaginales no se deben usar.

Dr. Isaacs:

Estoy en parte de acuerdo con el Dr. Axtmayer, pero nosotros con frecuencia en nuestra práctica vemos a mujeres que vienen con ataque de cistitis y mayormente uretritis y estas mujeres presentan siempre secreciones vaginales y en el historial encontramos que el esposo padece de una prostatitis muchas veces es el medio de iniciar uno de estos ataques y uno de los métodos de prevención es la irrigación vaginal, sino inmediatamente después del coito al otro día.

Dr. Axtmayer:

Yo creo que es una cuestión de etiología. Vamos a ver, la paciente tiene tricomonas, tiene moniliasis, el esposo tiene una prostatitis debido a tricomona pues vamos a tratar triconomas, si es candidiasis tratamos candidiasis. Buscamos el factor etiológico y se da el tratamiento adecuado, ahora, el tratamiento de moniliasis y de triconomiasis no es la ducha vaginal sino el agente específico que liquida al agente que está causando esto, pero la ducha vaginal de por sí no la cura porque el organismo se queda ahí.

Dr. Cangiano:

Estamos de acuerdo que hay que tratar con terapia específica tanto al esposo como a la esposa y ese es el

punto. Para finalizar yo quisiera preguntarle al Dr. Bermúdez, ¿qué hay de nuevo en infecciones urinarias, específicamente con infecciones por pseudomonas?

Dr. Bermúdez:

Necesitamos un agente contra la pseudomona que se pueda dar oralmente. Próximamente estará disponible este agente para el uso rutinario de estas infecciones.

SOBRE LA NUEVA CUBIERTA

— INVITACION —

**LA JUNTA EDITORA INVITA CORDIALMENTE A TODOS,
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PORTADA DEL BOLETIN DE LA ASOCIACION MEDICA DE
PUERTO RICO.**

**Jorge O. Just Viera, MD
Editor**

LAS INDICACIONES PARA AMIGDALECTOMIA

En Puerto Rico se extirpan anualmente miles de amígdalas palatinas y faríngeas. En su estudio de viabilidad de un hospital de niños, Flores-Gallardo analizó las admisiones de cinco hospitales generales del área metropolitana de San Juan en el 1971 encontrando que de 6,736 admisiones pediátricas 1,724, o sea el 25.5 por ciento, eran para amigdalectomía y adenoidectomía. Los gastos de estas intervenciones en todo Puerto Rico se pueden medir en cientos de miles de dólares. La morbilidad y mortalidad de las mismas no se conoce en Puerto Rico pero en Estados Unidos se informan sobre 300 muertes al año y se han descrito numerosas complicaciones. El Dr. Sylvan E. Stool, en esta edición del Boletín, presenta sus acertados puntos de vista sobre dichas operaciones y llama la atención a una precaución poco conocida para evitar posibles defectos del habla como consecuencia de la adenoidectomía.

La inflamación e hipertrofia de las amígdalas faríngea y palatinas forman parte de las infecciones respiratorias en los niños. Niños normales tienen un promedio de cinco a seis infecciones respiratorias agudas anualmente. La mayoría son virales, otras de origen bacteriano, pero ordinariamente no son debidas a que el niño tiene amígdalas. Muchas veces se atribuyen incorrectamente a las amígdalas manifestaciones respiratorias alérgicas. Con cada infección respiratoria se agrandan las amígdalas, las cuales muy gradualmente vuelven a su tamaño normal, que en casi todos los niños hasta la adolescencia están hipertrofiadas. Las infecciones respiratorias de origen exógeno no se evitan mediante amigdalectomías o adenoidectomías; por otra parte, es muy raro encontrar una infección bacteriana de las amígdalas que no pueda curarse con tratamiento antimicrobiano adecuado.

Actualmente no se consideran las amígdalas como foco de infección que debe extirparse para evitar enfermedades generales. Por lo general, no se recomiendan la amigdalectomía y adenoidectomía en: (1) niños menores de tres años (2) rinitis recurrente (3) hipertrofia de las amígdalas (4) artritis (5) nefritis (6) fiebre reumática (7) durante brotes de polio (8) tuberculosis.

Las indicaciones para amigdalectomía o adenoidectomía pueden ser diferentes. Están indicadas una u otra operación, o ambas en las siguientes afecciones: (1) Absceso peritonsilar, (2) Hipertensión pulmonar o cor pulmonale por obstrucción de las vías respiratorias altas. (3) Hábito adenoideo con deformidad torácica por obstrucción crónica. Cuando se considera el problema de obstrucción a la respiración debe recordarse que muchas veces ésta se debe a alergias de origen nasal que no se aliviarán con una adenoidectomía. (4) Infección por gérmenes resistentes a los antimicrobianos y manifestaciones clínicas graves recurrentes. (5) Infección por difteria persistente por más de tres meses a pesar de tratamiento adecuado con antimicrobianos. (6) Manifestaciones clínicas persistentes de alteraciones de la audición, otitis media, rinitis purulenta y sinusitis, a pesar de tratamiento adecuado, claramente debidas a vegetaciones adenoideas. La resección de las vegetaciones adenoideas sin extirpar las amígdalas faríngeas puede ser la operación de elección en estos casos. Esto tiene importancia práctica porque conlleva una disminución de morbilidad y mortalidad y una menor interferencia con la función inmunológica de estos tejidos.

Antes de la operación se debe efectuar una cuidadosa evaluación de cada enfermo sin olvidar pruebas para descartar fiebre reumática, cardiopatías, tuberculosis y coagulopatías. Las complicaciones más importantes de la operación, exceptuando accidentes anestésicos, son: hemorragias, aspira-

ción de sangre y coágulos, abscesos pulmonares, neumonías y sepsis. Se ha sospechado interferencia con los procesos inmunológicos normales y se han observado disminuciones en los niveles de anticuerpos contra polio en niños vacunados antes de la operación. Estudios por inmunofluorescencia de amígdalas crónicamente infectadas han demostrado que éstas producen grandes cantidades de inmunoglobulinas tipo G y menores proporciones de IgA e IgM. Se ha informado, además, que por contribuir estos tejidos linfáticos a ocupar un espacio durante el crecimiento y desarrollo, su extirpación puede afectar el normal desarrollo facial y de las vías respiratorias altas. Según apunta Stool, en ciertos niños las amígdalas faríngeas son necesarias para la fonación normal. Estos tienen un paladar blando corto que, en la ausencia de tejido adenoideo, no logra tocar la faringe posterior lo que es necesario para emitir ciertos sonidos. El resultado postoperatorio puede ser defecto del habla. Otra complicación informada por Stool es pérdida de audición por otitis serosa.

Si las indicaciones para amigdalectomía en nuestro ambiente fueran tan rigurosas como las que presenta el Profesor de Otorrinolaringología de Filadelfia, Sylvan Stool, es probable que habría una notable reducción en el número de dichas operaciones en Puerto Rico y, como resultado, importantes ahorros en mortalidad, morbilidad y dinero. Indudablemente muchas amigdalectomías y adenoidectomías se hacen por aparente hipertrofia de las amígdalas solamente o por presiones de familiares, maestros, y hasta políticos antes que por verdaderas indicaciones científicamente establecidas.

La amigdalectomía y la adenoidectomía son operaciones que pueden efectuarse rápidamente pero no son sencillas ni están exentas de complicaciones graves. La alta frecuencia con que se efectúan estas operaciones tanto en Puerto Rico como en Estados Unidos, sugiere la necesidad de una mejor selección de los casos. Las facultades de los hospitales tienen los medios de modificar dicha selección estableciendo criterios y exigiendo un proceso adecuado de consulta antes de autorizar cada operación. Esto se ha hecho para otras intervenciones quirúrgicas con resultados satisfactorios, sería de gran beneficio para los niños afectados y probablemente contribuiría a aliviar la escasez de camas en los hospitales y el alto costo de los servicios de salud.

José E. Sifontes, MD

CARTA AL EDITOR

Dr. Jorge O. Just Viera, Editor
Boletín de la Asociación Médica de P. R.
Santurce, Puerto Rico

Estimado doctor Just:

Le incluyo un comunicado, a nombre de la Sección que presido, para su consideración como editor del Boletín.

Interesamos que de contar con la aprobación de la Junta Editora, se publique dicha información próximamente en el Boletín.

Muchas gracias por su cooperación.

*Francisco Aguiló, Jr., MD, Presidente
Sección de Endocrinología y Diabetes
Asociación Médica de Puerto Rico*

LA NUEVA INSULINA "U-100"

El año 1973 marca un nuevo paso en el tratamiento del paciente con diabetes mellitus que requiere la administración de insulina. Se trata de la nueva insulina "U-100", o sea, la que contiene 100 unidades por mililitro (100U/cc), y que viene a suplantar las tradicionales insulinas U-40 y U-80 con las cuales todos tenemos familiaridad.

En el número de Julio de 1972 de la revista "Diabetes", órgano oficial de la Asociación Americana de Diabetes, se publicó esta decisión, adoptada el 23 de junio de 1972 por la Junta de Directores de dicha Asociación la cual fue preparada por el Comité sobre el uso de Agentes Terapéuticos de la misma.

Esta decisión responde a varias razones de índole práctica, a saber: (1) errores frecuentes al medir la insulina en fracciones de mililitro usando un sistema que no es decimal; (2) errores al medir insulina "U-40" en

jeringuillas con escala de "U-80" y vice-versa; (3) incertidumbre de medidas de insulina hechas en jeringuillas de escala doble, sujeto al error apuntado en el número (2); (4) la gran ventaja de un sistema con base 100, en el cual las unidades coincidirán con el volumen correspondiente en la jeringuilla.

Se espera que lo más pronto posible pueda establecerse el uso de la nueva insulina, la cual ya está en el mercado. Dicha insulina se ofrecerá en los mismos tipos (acción corta y acción prolongada) que han estado disponibles hasta ahora.

Requiere, sin embargo, que las jeringuillas "U-100" correspondientes estén ampliamente disponibles en farmacias y hospitales.

A la clase médica nos corresponde la labor de re-educar dichos pacientes. A estos se les deberá explicar claramente que el cambio en el tipo de insulina *requiere la nueva jeringuilla U-100*, pero que *no envuelve cambio alguno en su dosis usual de insulina*: por ejemplo, 40 unidades de insulina U-40 o U-80 tendrán la misma potencia terapéutica de 40 unidades de "U-100", excepto que al medirla, deberá llevar el émbolo a una posición que no corresponde a ninguna de las dos insulinas tradicionales (o sea hasta la marca de 1cc para jeringuillas de U-40 o hasta la mitad de la jeringuilla para U-80), sino, naturalmente, hasta donde indique el número "40", y que será correspondiente a 0.4ml.

Para pacientes usando cantidades pequeñas de insulina (como es el caso del paciente juvenil), habrá una jeringuilla especial más angosta, de solo 35 unidades (.35ml de capacidad) donde sea fácil el medir tales dosis bajas con precisión.

Exhortamos a los médicos y al personal para-médico a cooperar en la orientación del paciente diabético en este particular para lograr la uniformidad deseada en la dosificación de la insulina.

SALE OR DISPOSITION OF A MEDICAL PRACTICE

(Prepared by The Office of the General Counsel of the American Medical Association)

NARCOTICS

Narcotics and other "Dangerous Drugs" is another special area of concern, both State and Federal Statutes govern the dispensing of narcotics and other "Dangerous Drugs". The physician will certainly be registered under the provisions of the Federal law; he will have been issued a Certificate of Registration bearing his name, and a Registration Number will have been assigned to him. This "Certificate of Registration" is required by law to be posted in a conspicuous place in his office. This Certificate of Registration must be returned to the Director of the Bureau of Narcotics and Dangerous Drugs, who will cancel same and return it. It must then be retained with all other records relating to narcotics and dangerous drugs for a period of not less than two years.

The doctor obtains narcotics or other "Controlled Substances", as the law refers to them, by ordering from a registered supplier on Official Order Forms bearing the registration number of the ordering physician. These Official Order Forms are obtained from the Bureau of Narcotics and Dangerous Drugs in limited quantities by requisition. Any of these Official Order Forms which are unused by the doctor at the time his "Certificate of Registration" is returned for cancellation, must also be returned to the Bureau of Narcotics and Dangerous Drugs. This is very important, because the Official Order Form bears the registration number of the doctor and is relied upon by the supplier to authenticate the purchase of the narcotics and other "Controlled Substances" described on the form.

The other records referred to above, which must be retained for a period of not less than two years, consist of the following:

1. The annual application for a Certificate of Registration.
2. Inventory of all narcotics and other Controlled Substances on hand. An inventory is required to be taken and filed with the Bureau of Narcotics and Dangerous Drugs every two (2) years.
3. Duplicate copies of the Official Order Forms which the doctor used to obtain narcotics and other Controlled Substances.
4. The physician's daily record of dispensing narcotics and other Controlled Substances.

The foregoing records will provide a close and accurate accounting of all of the narcotics and "Dangerous Drugs" handled by the physician, and will indicate the amount of narcotics and "Dangerous Drugs" which the doctor should have on hand. These records must be available for inspection by Federal agents at all times.

The narcotics and "Dangerous Drugs" on hand may be sold to the physician purchasing the practice by using the order forms to record the transaction, but only after obtaining specific approval of the Regional Director of the Bureau of Narcotics and Dangerous Drugs. If the purchasing doctor is properly registered, the approval will be forthcoming. Incidentally, the purchasing physician will have to file a new application for registration and obtain a "Certificate of Registration" for his new location if he is taking over the selling physician's office.

If for some reason the narcotics or other "Controlled Substances" which the doctor has on hand are not sold, Federal Regulations require that the Regional Director of the Bureau of Narcotics and Dangerous Drugs be notified, and he in turn will issue instructions on the manner of their disposal.

1. They may be delivered to the Bureau of Narcotics and Dangerous Drugs. No compensation is paid, but a tax refund may be obtained in certain instances.
2. They may be destroyed if so authorized, but only in the presence of an agent of the Bureau of Narcotics and Dangerous Drugs.

Regulations under the Federal law, known as the "Controlled Substances Act", which are referred to above, become effective October 1, 1971. Additional regulations may be anticipated as further experience is gained under this legislation. Further information can be obtained by writing to the Bureau of Narcotics and Dangerous Drugs, Department of Justice, Post Office Box 28083, Central Station, Washington, D. C., 20005.

Non-narcotic drugs which are not subject to Federal or State laws, and which the physician may have on hand may be sold to the purchasing physician just as any other type of supplies which are included in the sale. If for some reason the purchasing physician does not wish to acquire the supply of drugs, the unopened containers can usually be returned to the drug supplier for credit. Care should be taken in the disposition of those drugs which have been opened and partially used; they should not be abandoned in such a way that the drugs may be misused. They may be donated to charitable organizations, and the doctor's local medical society may be helpful in suggesting proper organizations to receive them and arranging for distribution. *(To be continued)*

OPINIONES

Boletín Asociación Médica de Puerto Rico
P. O. Box 9387
Santurce, Puerto Rico 00908

Editor:

En la sección Opiniones de la edición del Boletín de marzo de 1973, aparece publicada bajo la firma del Dr. José Rodríguez Pastor una historieta alegórica sobre "la Asociación Médica de Villaturbia" (que de alegoría tiene muy poco) obviamente refiriéndose a la situación que, sobre salud, reina en la Insula Barataria (que de barata tiene menos). Me he dispuesto a comentar su escrito porque creo conocer esa historia y porque la información que brinda es tan incompleta que fácilmente lleva a uno hacia interpretaciones erróneas en perjuicio de los miembros de esa asociación.

Para comenzar diré que cuando el Dr. Rodríguez Pastor escribe que "todo lo que se hacía en la Asociación de Villaturbia, era una copia exacta de lo que se hacía en Homokan" claramente menosprecia la capacidad intelectual y la iniciativa individual, injustificadamente, de los miembros y de los directores de esa asociación. A lo mejor nuestro prestigioso colega se está refiriendo a otra Asociación Médica de Villaturbia porque la que yo conozco (que debió ser llamada Villadiáfana) NUNCA hizo algo por el mero hecho de copiarlo de la "Homokan Medical Association", a la cual todavía está afiliada. Cuando los médicos de Villaturbia decidieron establecer el sistema de los presidentes entrante, activo y saliente fue porque se consideró mucho más práctico y eficiente que el sistema de traer un hombre a la presidencia sin haber tenido la oportunidad de conocer previamente los problemas que existían en la asociación y los programas que se habían puesto en operación.

Obviamente el Dr. Rodríguez Pastor no perteneció a la Asociación de Villaturbia, o si perteneció poca fue su participación en ella, de lo contrario, se hubiera enterado plenamente de la historia de los "retratos al óleo". Habrá siempre, y si no, debiera haberla habido, una pared honrosa donde exhibirlos ya que son de hombres que dieron sus energías, su salud y su tiempo para proteger la libertad profesional del médico (aunque éste

no fuera miembro de la Asociación) que finalmente redundaba en beneficio del cuidado de la salud de los villaturbanos.

Me extraña sobremanera el juicio que hace el Dr. Rodríguez Pastor sobre los médicos de Villaturbia. ¿Es que al convertirse en especialista, el médico tiende a olvidarse de "las ansiedades y angustias de su pueblo"? ¿Es que por el hecho de ser especialista, el médico se torna en uno falto de caridad? ¿En que se basa el Dr. Rodríguez Pastor para señalar que existían esas faltas en esos médicos? ¿Es su historia alegoría o leyenda?

En la Asociación Médica de Villaturbia (la que yo conocí) NUNCA se le exigió a asambleísta alguno hablar en inglés o en español. Eso siempre se consideró prerrogativa del que iba a hablar. Si alguien "pidió permiso para hablar en español" lo hizo porque ignoraba que no tenía necesidad ni obligación alguna de hacerlo. Quien dice lo contrario está faltando a la verdadera historia de esa asociación.

Sobre el tema del "Seguro de Salud Universal" basta con decir que la Asociación Médica de Villaturbia ha sido la UNICA organización que desde hace años viene presentando "nuevos enfoques" sostenidos con planes abarcadores de servicios y con sistemas de financiamiento. Estas propuestas se llevaron a cabo en los años 1961, 1962, 1963, 1964 y 1967. Algunos de estos planes no solamente no fueron copiados de organización alguna sino que fueron establecidos en la Insula Barataria por primera vez en el mundo. De hecho, un miembro del "Homokan Medical Association" publicó un artículo felicitando a los médicos de Villaturbia porque se habían anticipado, en la solución de los problemas traídos por los altos costos de los servicios médico-hospitalarios, a la organización a la cual estaban afiliados. Este artículo se publicó en el "New England Journal of Medicine 268: 83 January 10, 1963". El autor principal fue Walter A. Noehren M. D. y esto no es ni alegoría ni fábula.

Lo que ha sucedido en la Insula Barataria es que los enfoques que se han querido implantar para resolver estos problemas han sido dirigidos más bien hacia el control del médico y del hospital que hacia el rendimiento de servicios médicos de la más alta calidad. Los mé-

dicos de Villaturbia, conscientes de su primordial deber a su pueblo, no pueden estar de acuerdo con estos enfoques.

El sistema que finalmente se implante tendrá que "copiar" algo de otros sistemas. Es casi imposible ser 100 por ciento original. Pero, como médico de Villaturbia, me tomo la libertad de decirle al Dr. Rodríguez Pastor que la solución no está en "copiar" del sistema fracasado

de la Insula Bloody-Jolly-Show. Abrigo la esperanza de que nuestro prestigioso amigo y colega también lo crea así.

Atentamente,

José M. Torres-Gómez, MD

ARTICULOS APROBADOS

1. Seasonal Patterns of Births in Puerto Rico — Ishver S. Bangdiwala MD and Abelardo Fuertes de la Haba.
2. Emergency Medical Care and Traffic Fatalities in Puerto Rico — Stephan H. Fromm, MD, FACS, and Gustavo A. Escalera, MD.
3. Hipotiroidismo y Desarrollo Sexual Precoz - Reporte de un Caso — Adolfo Pérez Comas, MD.
4. Ausencia Congénita de los Músculos Abdominales - "Prune Belly" — Reporte de un Caso — Luis C. Nina Ortega, MD y José R. Avila, MD.

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2. Burroughs Welcome Co. — Neosporin
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6. Roche — Dalmane, Efudex, Librium, Valium
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9. Smith, Kline & French — Dyazide
10. Stuart Pharmaceuticals — Mylanta
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12. Upjohn — Unicap Therapeutic

NOTICIAS

AMA NEWS RELEASE:

CAUTION URGED IN HAIR TRANSPLANTS

CHICAGO — The hair transplant operation is a reliable panacea for baldies, but be careful — you might wind up with a hairline like Dracula.

This admonition is voiced in the current (March) issue of *Archives of Otolaryngology*, a scientific journal of the American Medical Association.

Actually, the advice is directed to physicians who perform the hair transplants. It urges very careful advance planning and careful use of the proper, tested surgical techniques in performing hair transplants.

The report is by Charles M. Monell, MD., and Walter E. Berman, MD., of the division of head and neck surgery of the University of California at Los Angeles School of Medicine.

In the transplant procedure, small tufts of skin and hair are removed from the back of the neck and replanted on the front of the scalp where baldness has occurred. The transplanted hairs then grow longer and, in time, cover the bald spots.

"It is a technique of great promise, but much of the promise is not being realized. It is not the fault of the procedure, the blame must be directed at the person doing the job," the authors say.

"Unfortunately, the results are often not good, and many patients have suffered severe emotional and physical scars."

"Doctors are devising new hair lines seldom seen in nature. One was the creation of a dermatologist who conceived an inverted triangle coming to a sharp point low in the center of the forehead. The effect was tragic. After intense searching, we did find one man who had such a hairline. It was the creation of a make-up artist for Bella Lugosi as Count Dracula, in a film called 'The White Zombie'."

THE ANNUAL OTOLARYNGOLOGY ASSEMBLY OF 1973 will be held October 20 through 26, 1973, in the Eye and Ear Infirmary of the University of Illinois Hospital. The Department of Otolaryngology of the Abraham Lincoln School of Medicine, University of Illinois at the Medical Center, offers a condensed basic and clinical program for practicing otolaryngologists under the direction of Emanuel M. Skolnik, MD, with Burton J. Soboroff, MD, as co-chairman. This program is designed to bring to specialists current information in medical and surgical otorhinolaryngology.

Interested otolaryngologists should direct their inquiries to the mailing address: OTOLARYNGOLOGY, P. O. Box 6998, Chicago, Ill., 60680.

COARSE IN LARYNGOLOGY AND BRONCHOSOPHAGOLGY — The Department of Otolaryngology, Abraham Lincoln School of Medicine of the University of Illinois and the Eye and Ear Infirmary of the University of Illinois Hospital,

will conduct a continuing education course in Laryngology and Bronchoesophagology November 12 to 17, 1973. The course is limited to twenty physicians and will be under the direction of Paul H. Holinger, MD. It will be held largely at the Eye and Ear Infirmary, 1855 West Taylor Street, Chicago, and will include visits to a number of other Chicago hospitals. Instruction will be provided by means of animal demonstrations and surgical clinics, as well as didactic lectures.

Interested physicians will please write directly to the Department of Otolaryngology, Eye and Ear Infirmary, 1855 West Taylor Street, Chicago, Illinois 60612.

CHAMPUS NEWS — From the Office for Civilian Health and Medical Program of the Uniformed Services, Denver, Colorado, 80240.

CHAMPUS OFFICIALS ISSUE FULL PAYMENT CONCEPT REMINDER.

DENVER — The full payment provisions of CHAMPUS protect the beneficiary from paying for disallowed charges when physicians or other providers of care agree to participate in the Civilian Health and Medical Program of the Uniformed Services.

That protection under the full payment concept, CHAMPUS officials say, does not automatically extend to consulting physicians, assistant surgeons, anesthetics and other health care team members who are working with a participating physician.

Traditionally assistant surgeons, anesthetists and consulting physicians bill for their services independently and therefore they may choose not to participate in CHAMPUS. If they do not participate the CHAMPUS beneficiary loses the protection of the full payment provisions.

Beneficiaries who suspect that their attending physician will be using assistant surgeons, anesthetists or consulting physicians should attempt to insure that all such personnel also agree to participate in CHAMPUS.

NEWS RELEASE from The American Academy of Pediatrics.


HIGHER DOSES OF AMPHETAMINES MAY CAUSE GROWTH SUPPRESSION IN CHILDREN.

EVANSTON, ILL. — The long-term use of certain drugs in the treatment of hyperactive children can lead to "a highly significant suppression of growth in weight and height," two researchers have reported in the April issue of *Pediatrics*, the monthly scientific journal of the American Academy of Pediatrics.

Daniel J. Safer, M.D., and Richard P. Allen, Ph.D., said the study of 63 hyperactive children indicated that the amount of growth suppression depended on the type of drug given, the amount of the dose, and the frequency of use.

Integument!

Our skin—the human integument—covers us, defines us, protects us. But skin is subject to cuts, burns, abrasions. And infections. Neosporin Ointment fights infection by providing broad antibacterial action against susceptible skin invaders. It contains antibiotics that are rarely used systemically, reducing the risk of sensitization.



INDICATIONS: *Therapeutically*, used as an adjunct to appropriate systemic therapy for topical infections, primary or secondary, due to susceptible organisms, as in:

- infected burns, skin grafts, surgical incisions, otitis externa
- primary pyodermas (impetigo, ecthyma, sycosis vulgaris, paronychia)
- secondarily infected dermatoses (eczema, herpes, and seborrheic dermatitis)
- traumatic lesions, inflamed or suppurating as a result of bacterial infection.

Prophylactically, the ointment may be used to prevent bacterial contamination in burns, skin grafts, incisions, and other clean lesions. For abrasions, minor cuts and wounds accidentally incurred, its use may prevent the development of infection and permit wound healing.

CONTRAINDICATIONS: Not for use in the external ear canal if the eardrum is perforated. This product is contraindicated in those individuals who have shown hypersensitivity to any of the components.

PRECAUTION: As with other antibiotic preparations, prolonged use may result in overgrowth of nonsusceptible organisms and/or fungi. Appropriate measures should be taken if this occurs. Articles in the current medical literature indicate an increase in the prevalence of persons allergic to neomycin. The possibility of such a reaction should be borne in mind.

Complete literature available on request from Professional Services Dept. PML.

NEOSPORIN[®] Ointment

(POLYMYXIN B-BACITRACIN-NEOMYCIN)

Each gram contains: Aerosporin[®] brand Polymyxin B Sulfate 5,000 units; zinc bacitracin 400 units; neomycin sulfate 5 mg. (equivalent to 3.5 mg. neomycin base); special white petrolatum q.s. In tubes of 1 oz. and ½ oz. and ¼ oz. (approx.) foil packets.



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Only Maalox[®] has been added to help protect the intolerant

Ascriptin is for those patients who suffer from gastric intolerance due to aspirin. One Ascriptin tablet combines 150 mg. of Maalox with 5 grains of aspirin to help reduce aspirin-induced gastric distress. When the symptoms of flu occur, specify Ascriptin... classic flu management—improved.



Ascriptin[®]—the Maalox[®]-protected aspirin

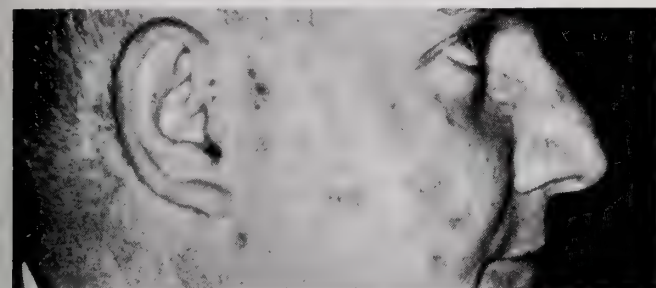
**What's
on your
patient's
face...**

**may be more important than
his chief complaint**

The lesions on his face may be solar/actinic — so-called 'senile' keratoses...and they may be premalignant.

Solar, actinic or senile keratoses

These lesions may be called by several names, but they usually can be identified by the following characteristics: the typical lesion is flat or slightly elevated, of a brownish or reddish color, papular, dry, rough, adherent, and sharply defined. They commonly occur as multiple lesions, chiefly on the exposed portions of the skin.



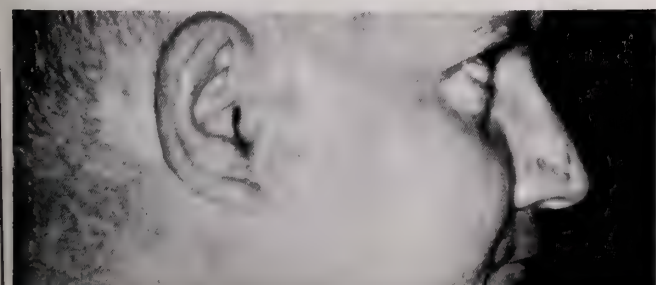
Patient P.T. seen on 3/29/67 shows typical lesions of moderately severe keratoses. Note residual scarring on ridge of nose from previous cryosurgical and electro-surgical procedures.*

Sequence of therapy/ selectivity of response

After several days of therapy with Efudex® (fluorouracil), erythema may begin to appear in the area of the lesions; the reaction usually reaches its height of unsightliness and discomfort within two weeks, declining after discontinuation of therapy. This reaction occurs in affected areas. Since the response is so predictable, lesions that do not respond should be biopsied.

Acceptable results

Treatment with Efudex provides highly favorable cosmetic results. Incidence of scarring is low. This is particularly important with multiple facial lesions. Efudex should be applied with care near the eyes, nose and mouth.



Patient P.T. seen on 6/12/67, seven weeks after discontinuation of 5%-FU cream. Reaction has subsided. Residual scarring not seen except for that due to prior surgery. Inflammation has cleared and face is clear of keratotic lesions.*

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Multiple actinic or solar keratoses.

Contraindications: Patients with known hypersensitivity to any of its components.

Warnings: If occlusive dressing used, may increase inflammatory reactions in adjacent normal skin. Avoid prolonged exposure to ultraviolet rays. Safe use in pregnancy not established.

Precautions: If applied with fingers, wash hands immediately. Apply with care near eyes, nose and mouth. Lesions failing to respond or recurring should be biopsied.

Adverse Reactions: Local — pain, pruritus, hyperpigmentation and burning at application site most frequent; also dermatitis, scarring, soreness and tenderness. Also reported — insomnia, stomatitis, suppuration, scaling, swelling, irritability, medicinal taste, photosensitivity, lacrimation, leukocytosis, thrombocytopenia, toxic granulation and eosinophilia.

Dosage and Administration: Apply sufficient quantity to cover lesion twice daily with non-metal applicator or suitable glove. Usual duration of therapy is 2 to 4 weeks.

How Supplied: Solution, 10-ml drop dispensers — containing 2% or 5% fluorouracil on a weight/weight basis, compounded with propylene glycol, tris(hydroxymethyl)aminomethane, hydroxypropyl cellulose, parabens (methyl and propyl) and disodium edetate.

Cream, 25-Gm tubes — containing 5% fluorouracil in a vanishing cream base consisting of white petrolatum, stearyl alcohol, propylene glycol, polysorbate 60 and parabens (methyl and propyl).

**This patient's lesions
were resolved with**

**Efudex[®]
(fluorouracil)**

**5% cream/solution
...a Roche exclusive**



Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, N.J. 07110

*Data on file, Hoffmann-La Roche Inc., Nutley, N.J.

We're not against all her E. coli...

only the E. coli in her
urinary tract



Macrochantin (nitrofurantoin macrocrystals) is exceptionally effective against E. coli. But it confines its antibacterial action to the urinary tract. It is indicated for the treatment of cystitis,* pyelitis* and pyelonephritis*...nothing else.

Macrochantin is not indicated for therapy of any systemic infection. *And it does not suppress normal bac-*

**Basic in cystitis*, pyelitis*,
pyelonephritis***

The one-tract action of

Macrochantin® Capsules
(nitrofurantoin macrocrystals) 50mg./100mg.

Indications: Macrochantin (nitrofurantoin macrocrystals) is indicated for the treatment of pyelonephritis, pyelitis and cystitis due to E. coli, enterococci, Staph. aureus or a small percentage of strains of Pseudomonas, when demonstrated to be susceptible by in vitro susceptibility testing. Also for treatment of such infections when due to some susceptible strains of Klebsiella-Aerobacter and Proteus. It is not indicated for treatment of associated renal cortical or perinephric abscesses, systemic infections or prostatitis, or in any genitourinary tract infections other than pyelonephritis, pyelitis and cystitis.

Contraindications: Anuria, oliguria or extensive impairment of renal function is a contraindication. The drug is contraindicated for infants under one month and in pregnant patients at term. The drug should not be administered to persons who have shown hypersensitivity to nitrofurantoin.

Warnings: Macrochantin may cause hemolytic anemia of the primaquine sensitivity type, apparently linked to a glucose-6-phosphate dehydrogenase deficiency. This deficiency is found in 10 per cent of Negroes and in a small percentage of ethnic groups of Mediterra-

nean and Near-Eastern origin. Such patients should be observed closely while receiving nitrofurantoin. Discontinue the drug at any sign of hemolysis. Hemolysis ceases on withdrawal. Superinfections may occur, most commonly due to Pseudomonas.

Usage in pregnancy: THE SAFETY OF NITROFURANTOIN DURING PREGNANCY AND LACTATION HAS NOT BEEN ESTABLISHED. IT SHOULD NOT BE USED IN WOMEN OF CHILDBEARING POTENTIAL UNLESS THE EXPECTED BENEFITS OUTWEIGH THE POSSIBLE HAZARDS.

Precautions: Peripheral neuropathy may occur. A fatality has been reported. Predisposing conditions such as renal impairment, anemia, diabetes, electrolyte imbalance, vitamin B deficiency and debilitating disease may enhance such occurrence.

Adverse reactions: Nausea, emesis and diarrhea may occur; reduction in dosage may alleviate these symptoms. Sensitization appearing as cutaneous eruptions or pruritus has occurred. Hypersensitivity reactions resulting in nonfatal anaphylaxis, angioedema, pulmonary infiltration with pleural effusion and eosinophilia have been reported. Other possible

terial flora elsewhere in the body. (As with other antibacterials, superinfections may occur, but these are limited to the urinary tract. Pseudomonas is the organism most commonly implicated.)

Macrochantin works against a majority of urinary tract pathogens, including some strains of Proteus and Klebsiella-Aerobacter; however, only a small percentage of strains of Pseudomonas are susceptible.

*Due to susceptible organisms

reactions are chills, fever, jaundice, asthmatic symptoms and hypotension. Occasionally headache, dizziness, nystagmus, vertigo, drowsiness, malaise and muscular aches have occurred. Transient alopecia has been reported. Leukopenia, including granulocytopenia, has been reported rarely. The blood picture has returned to normal following cessation of therapy. As with other antimicrobial agents, superinfections by resistant organisms may occur. With Macrochantin, however, these are limited to the genitourinary tract because suppression of normal bacterial flora elsewhere in the body does not occur.

Dosage: Adult: 50 to 100 mg. four times a day.

Supplied: Macrochantin (nitrofurantoin macrocrystals) Capsules of 50 mg. and 100 mg.

EATON PRODUCT CODE—For easy product identification and verification—Macrochantin Capsules 50 mg. (F03), 100 mg. (F04).



Originators and Developers of The Nitrofurans
EATON LABORATORIES
Norwich International
410 Park Avenue, New York, N.Y. 10022

Cuando comen lo que les gusta
y no lo que deben...



ayude a cubrir "el déficit" de vitaminas con

Unicap Therapeutic

10 vitaminas combinadas con 7 minerales

Cada tableta contiene:

Vitamina A	1.5 mg.
Vitamina D	10 mcg.
Mononitrato de Tiamina (B-1)	10 mg.
Riboflavina (B-2)	10 mg.
Acido Ascórbico (C) (como ascorbato de sodio)	300 mg.
Niacinamida	100 mg.
Clorhidrato de Piridoxina (B-6)	2 mg.
Pantotenato de Calcio	20 mg.
Cobalamina (B-12) (como concentrado de cobalamina)	20 mg.
Vitamina E	30 Unidades Internacionales
Hierro (a partir de 50 mg. de sulfato ferroso)	10 mg.
Yodo (como yoduro de potasio)	0.15 mg.
Calcio (como carbonato)	50 mg.
Cobre (como sulfato)	1 mg.
Manganeso (como sulfato)	1 mg.
Magnesio (como sulfato)	6 mg.
Potasio (como sulfato)	5 mg.

Posología: Adultos y niños mayores de 6 años - 1 tableta diaria.

Presentación: Frascos de 30 y 90

Upjohn

PR 9226.1 MAY, 1969

6811 MARCA REGISTRADA EN E.U.A.; UNICAP THERAPEUTIC

UPJOHN INTER-AMERICAN CORPORATION / CAPARRA / PUERTO NUEVO

How strong must a tranquilizer be for severe anxiety?

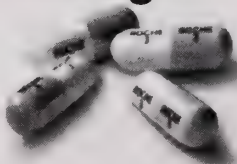
As strong as Librium® 25 mg (chlordiazepoxide HCl)



The achievement of desired therapeutic results is often a function of the dosage strength as well as the drug's intrinsic action. Thus, when anxiety is *severe*, the 25-mg strength of Librium frequently provides the necessary antianxiety action with a minimum of unwanted adverse reactions. Librium 25 mg is a convenient dosage form for the relief of severe, incapacitating anxiety, specifically formulated to supplement your counsel and reassurance.

Benefits-to-risks ratio permits higher dosage

For over 13 years, Librium has been recognized for its excellent benefits-to-risks ratio, an asset in the *higher* dosage ranges as in more common clinical applications. Thus, the frequency of dosage with Librium 25 mg can be flexibly adjusted to the needs and response of the individual patient, up to 100 mg daily if required. Total daily dosage for the elderly and debilitated should not exceed 20 mg. When severe anxiety has been reduced, Librium dosage should be correspondingly reduced or discontinued entirely.



basic support
in severe anxiety
Librium® 25 mg
(chlordiazepoxide HCl)
1 capsule t.i.d./q.i.d.



Roche Laboratories
Division of Hoffmann-La Roche Inc
Nutley, N.J. 07110

Before prescribing, please consult complete product information, a summary which follows:

Indications: Relief of anxiety and tension occurring alone or accompanying various states.

Contraindications: Patients with known hypersensitivity to the drug.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who may increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates have been reported. Use of any drug in pregnancy, lactation, or in women of childbearing age should have its potential benefits weighed against possible hazards.

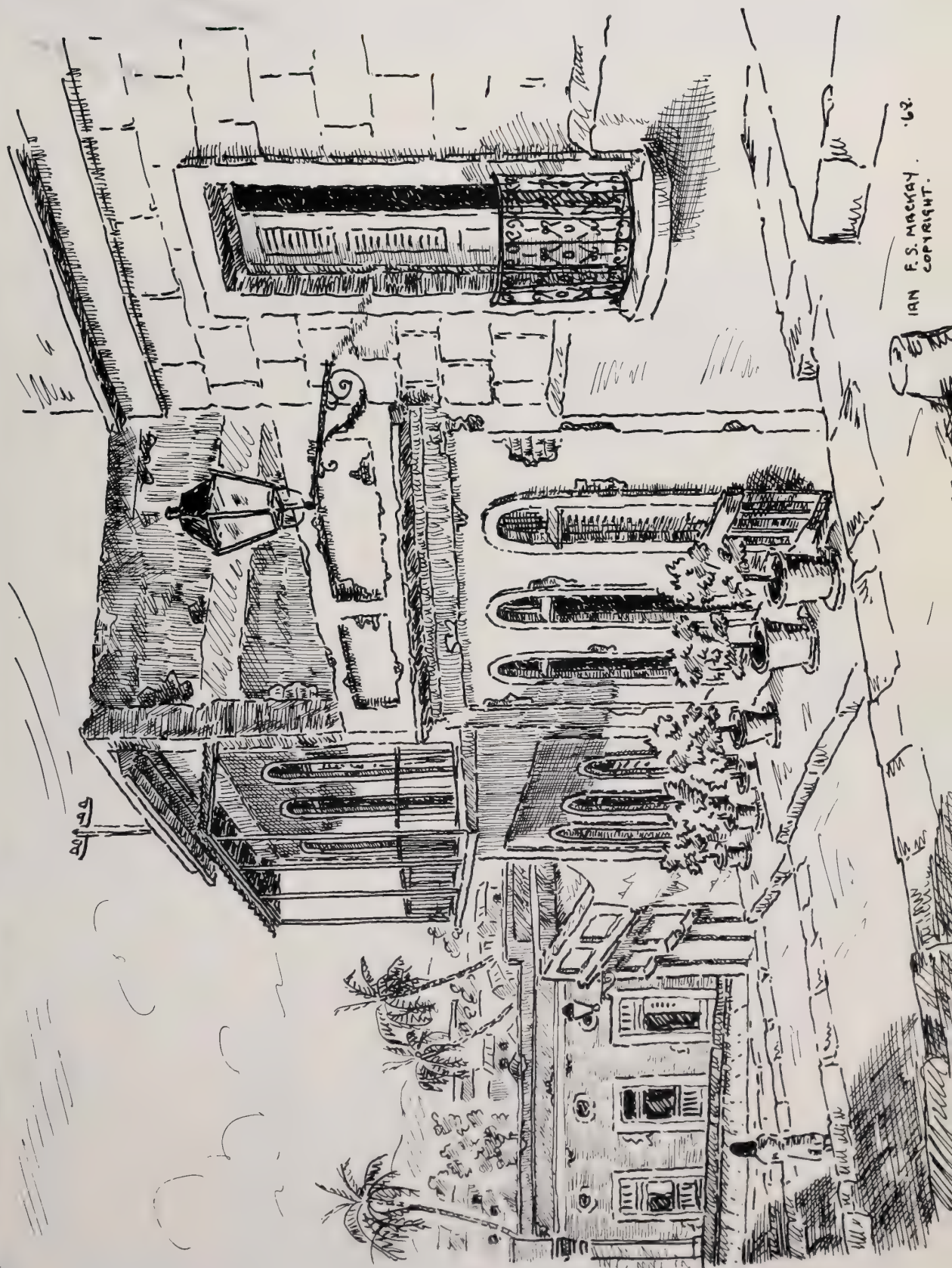
Precautions: In the elderly and debilitated and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of patients with evidence of impending depression; suicidal tendencies may be present and precautionary measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: Drowsiness, ataxia, confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage range. In a few instances syncope has been reported. A counteracted are isolated instances of skin edema, minor menstrual irregularities, nausea, constipation, extrapyramidal symptoms, and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally; periodic blood counts and liver function tests advisable during protracted therapy.

Supplied: Librium® Capsules containing 5 mg, 10 mg or 25 mg chlordiazepoxide HCl. Libritabs® Tablets containing 5 mg, 10 mg or 25 mg chlordiazepoxide.

DISPLAY
SHELVES

Mayo 1973
Vol. 65, No.5



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Everybody experiences psychic tension.



Most people can handle this tension.



Some people develop excessive psychic tension and need your counseling,



and a few may need counseling
and the psychotropic action of Valium® (diazepam).

Before deciding to make Valium (diazepam) part of your treatment plan, check on whether or not the patient is presently taking drugs and, if so, what his response has been. Along with the medical and social history, this information can help you determine initial dosage, the possibility of side effects and the ultimate prospects of success or failure.

While Valium can be a most helpful adjunct to your counseling, it should be prescribed only as long as excessive psychic tension persists and should be discontinued when you decide it has accomplished its therapeutic task. In general, when dosage guidelines are followed, Valium is well tolerated (see Dosage). For convenience it is available in 2-mg, 5-mg and 10-mg tablets.

Drowsiness, fatigue and ataxia have been the most commonly reported side effects.

Until response is determined, patients receiving Valium should be cautioned against engaging in hazardous occupations requiring complete mental alertness, such as driving or operating machinery.



Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, N.J. 07110

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anti-convulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

Dosage: Individualize for maximum beneficial effect.

Adults: Tension, anxiety and psychoneurotic states, 2 to 10 mg b.i.d. to q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed; adjunctively in skeletal muscle spasm, 2 to 10 mg t.i.d. or q.i.d.; adjunctively in convulsive disorders, 2 to 10 mg b.i.d. to q.i.d. **Geriatric or debilitated patients:** 2 to 2½ mg, 1 or 2 times daily initially, increasing as needed and tolerated. (See Precautions.) **Children:** 1 to 2½ mg t.i.d. or q.i.d. initially, increasing as needed and tolerated (not for use under 6 months).

Supplied: Valium® (diazepam) Tablets, 2 mg, 5 mg and 10 mg; bottles of 100 and 500. All strengths also available in Tel-E-Dose® packages of 1000.

Valium® (diazepam)

To help you manage excessive psychic tension



Organo Oficial Fundado en 1903

Volumen 65 Mayo 1973 Número 5

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Second Class postage paid at San Juan, P. R.

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Sally's back in sew biz! After an arthritic flare-up.

Butazolidin® alka Geigy

Each capsule contains:

100 mg. phenylbutazone USP

100 mg. dried aluminum hydroxide gel USP

150 mg. magnesium trisilicate USP

If it doesn't work in a week, forget it.

including aplastic anemia, may occur suddenly despite regular hemograms, and may become manifest days or weeks after cessation of drug. Any significant change in total white count, relative decrease in granulocytes, appearance of immature forms, or fall in hematocrit should signal immediate cessation of therapy and complete hematologic investigation. Unexplained bleeding involving CNS, adrenals, and G.I. tract has occurred.

The drug may potentiate action of insulin, sulfonamide, and sulfonamide-type agents. Carefully observe patients taking these agents. Nontoxic and toxic goiters and myxedema have been reported (the drug reduces iodine uptake by the thyroid). Blurred vision can be a significant toxic symptom worthy of a complete ophthalmological examination. Swelling of ankles or face in patients under sixty may be prevented by reducing dosage. If edema occurs in patients over sixty, discontinue drug.

Precautions: The following should be accomplished at regular intervals: Careful detailed history for disease being treated and detection of earliest signs of adverse reactions; complete physical examination including check of patient's weight; complete weekly (especially for the aging) or an every two week blood check; pertinent laboratory studies. Caution patients about participating in activity requiring alertness and coordination, as driving a car, etc. Cases of leukemia have been reported in patients with a history of short- and long-term therapy. The majority of these patients were over forty. Remember that arthritic-type pains can be the presenting symptom of leukemia.

Adverse Reactions: This is a potent drug; its misuse can lead to serious results. Review detailed information before beginning therapy. Ulcerative esophagitis, acute and reactivated gastric and duodenal ulcer with perforation and hemorrhage, ulceration and perforation of large bowel, occult G.I. bleeding with anemia, gastritis,

epigastric pain, hematemesis, dyspepsia, nausea, vomiting and diarrhea, abdominal distention, agranulocytosis, aplastic anemia, hemolytic anemia, anemia due to blood loss including occult G.I. bleeding, thrombocytopenia, pancytopenia, leukemia, leukopenia, bone marrow depression, sodium and chloride retention, water retention and edema, plasma dilution, respiratory alkalosis, metabolic acidosis, fatal and nonfatal hepatitis (cholestasis may or may not be prominent), petechiae, purpura without thrombocytopenia, toxic pruritus, erythema nodosum, erythema multiforme, Stevens-Johnson syndrome, Lyell's syndrome (toxic necrotizing epidermolysis), exfoliative dermatitis, serum sickness, hypersensitivity angitis (polyarteritis), anaphylactic shock, urticaria, arthralgia, fever, rashes (all allergic reactions require prompt and permanent withdrawal of the drug), proteinuria, hematuria, oliguria, anuria, renal failure with azotemia, glomerulonephritis, acute tubular necrosis, nephrotic syndrome, bilateral renal cortical necrosis, renal stones, ureteral obstruction with uric acid crystals due to uricosuric action of drug, impaired renal function, cardiac decompensation, hypertension, pericarditis, diffuse interstitial myocarditis with muscle necrosis, perivascular granulomata, aggravation of temporal arteritis in patients with polymyalgia rheumatica, optic neuritis, blurred vision, retinal hemorrhage, toxic amblyopia, retinal detachment, hearing loss, hyperglycemia, thyroid hyperplasia, toxic goiter, association of hyperthyroidism and hypothyroidism (causal relationship not established), agitation, confusional states, lethargy, CNS reactions associated with overdosage, including convulsions, euphoria, psychosis, depression, headaches, hallucinations, giddiness, vertigo, coma, hyperventilation, insomnia; ulcerative stomatitis, salivary gland enlargement. (B)98-146-070-G

Serious side effects do occur. Select patients carefully (particularly the elderly) and follow them closely in line with the drug's precautions, warnings, contraindications and adverse reactions.

For complete details, including dosage, please see full prescribing information

GEIGY Pharmaceuticals
Division of CIBA-GEIGY Corporation
Ardley, New York 10502

Important Note: This drug is not a simple analgesic. Do not administer casually. Carefully evaluate patients before starting treatment and keep them under close supervision. Obtain a detailed history, and complete physical and laboratory examination (complete hemogram, urinalysis, etc.) before prescribing and at frequent intervals thereafter. Carefully select patients, including those responsive to routine measures, contraindicated patients or those who cannot be observed frequently. Warn patients not to exceed recommended dosage. Short-term relief of severe symptoms with the minimum possible dosage is the goal of therapy. Dosage should be taken with meals or a full glass of milk. Sublingual capsules for tablets if dyspeptic symptoms occur. Patients should discontinue the drug and report immediately any sign of: fever, sore throat, oral lesions, symptoms of blood dyscrasia; dyspepsia, epigastric pain, symptoms of anemia, black or tarry stools or other evidence of intestinal ulceration or hemorrhage, skin reaction, significant weight gain or edema. A one-week trial period is adequate. Discontinue in the absence of a complete response. Restrict treatment periods to one week in patients over sixty.

Warnings: Acute gouty arthritis, rheumatoid arthritis, rheumatoid spondylitis

Contraindications: Children 14 years or less; senile past history or symptoms of G.I. inflammation or ulceration including severe, recurrent or persistent dyspepsia; history or presence of drug allergy; blood dyscrasias; renal, hepatic or cardiac dysfunction; hypothyroidism; thyroid disease; systemic edema; arthritis and salivary gland enlargement due to the disease; polymyalgia rheumatica and temporal arteritis; patients receiving other potent chemotherapeutic agents, or long-term anticoagulant therapy

Precautions: Age, weight, dosage, duration of therapy, extent of concomitant diseases, and concurrent potent therapy affect incidence of toxic reactions. Carefully instruct and observe the individual patient, especially the aging (forty years and over) who have increased susceptibility to the toxicity of the drug. Use the effective dosage. Weigh initially unpredictable risks against potential risk of severe, even fatal, results. The disease condition itself is unaltered by the drug. Use with caution in first trimester of pregnancy and nursing mothers. Drug may appear in cord blood and breast milk. Serious, even fatal, blood dyscrasias,

What should a medication for sleep be expected to provide?



Before prescribing Dalmane (flurazepam HCl), please consult Complete Product Information, a summary of which follows:

Indications: Effective in all types of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings and/or early morning awakening; in patients with recurring insomnia or poor sleeping habits; and in acute or chronic medical situations requiring restful sleep. Since insomnia is often transient and intermittent, prolonged administration is generally not necessary or

recommended.

Contraindications: Known hypersensitivity to flurazepam HCl.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. Caution against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Use in women who are or may become pregnant only when potential benefits have been weighed against possible hazards. Not recommended for use in persons under 15 years

of age. Though physical and psychological dependence have not been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage.

Precautions: In elderly and debilitated patients, initial dosage should be limited to 15 mg to preclude oversedation, dizziness and/or ataxia. If combined with other drugs having hypnotic or CNS depressant effects, consider potential additive effects. Employ usual precautions in patients who are severely depressed, or with

Sleep for 7 to 8 hours without need to repeat dosage during the night

No sleep medication has been as rigorously evaluated in the sleep research laboratory as Dalmane. Insomnia patients given one 30-mg capsule of Dalmane at bedtime, on average: fell asleep within 17 minutes, had fewer nighttime awakenings, spent less time awake after sleep onset, and slept for 7 to 8 hours with no need to repeat dosage during the night.

Sleep with consistency

Dalmane (flurazepam HCl) has been shown to be consistently effective even during consecutive nights of administration. Thus there is little likelihood for the need to increase dosage to maintain therapeutic effect.

Dalmane is in a class by itself. Not a narcotic, barbiturate or methaqualone, Dalmane is the only available benzodiazepine specifically indicated for insomnia.

Sleep with relative safety

Chronic tolerance studies have confirmed the relative safety of Dalmane (flurazepam HCl); no depression of cardiac or respiratory function was noted in patients administered recommended or higher doses for as long as 90 consecutive nights. In most instances when adverse reactions were reported they were mild, infrequent and seldom required discontinuance of therapy. Morning "hang-over" with Dalmane has been relatively infrequent. Dizziness, drowsiness, lightheadedness and the like have been the side effects noted most frequently, particularly in the elderly and debilitated. (An initial dose of Dalmane 15 mg should be prescribed for these patients.)

When your evaluation of insomnia indicates the need for a sleep medication, consider Dalmane—a single entity agent proved effective and relatively safe for relief of insomnia.

DALMANE[®]

(flurazepam HCl)

When restful sleep is indicated

One 30-mg capsule h.s. — usual adult dosage

(15 mg may suffice in some patients).

One 15-mg capsule h.s. — initial dosage for elderly or debilitated patients.

ROCHE

ROCHE LABORATORIES
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

nt depression or suicidal tendencies.
ndic blood counts and liver and kid-
function tests are advised during
eated therapy. Observe usual precau-
s in presence of impaired renal or
atic function.

Adverse Reactions: Dizziness, drowsi-
ess, lightheadedness, staggering, ataxia
falling have occurred, particularly
lterly or debilitated patients. Severe
ation, lethargy, disorientation and
na, probably indicative of drug intoler-
ce or overdosage, have been reported.

Also reported were headache, heart-
burn, upset stomach, nausea, vomiting,
diarrhea, constipation, GI pain, nervous-
ness, talkativeness, apprehension, irri-
tability, weakness, palpitations, chest
pains, body and joint pains and GU com-
plaints. There have also been rare occur-
rences of sweating, flushes, difficulty in
focusing, blurred vision, burning eyes,
faintness, hypotension, shortness of
breath, pruritus, skin rash, dry mouth,
bitter taste, excessive salivation, anorexia,
euphoria, depression, slurred speech.

confusion, restlessness, hallucinations,
and elevated SGOT, SGPT, total and direct
bilirubins and alkaline phosphatase.
Paradoxical reactions, e.g., excitement,
stimulation and hyperactivity, have also
been reported in rare instances.

Dosage: Individualize for maximum bene-
ficial effect. **Adults:** 30 mg usual dosage;
15 mg may suffice in some patients.
Elderly or debilitated patients: 15 mg
initially until response is determined.

Supplied: Capsules containing 15 mg or
30 mg flurazepam HCl.

"Prescription drugs – who should determine the maker?"

Dispenser of
Medicine

Clifton J. Latiolais
President
American
Pharmaceutical
Association



Maker of
Medicine

C. Joseph Stetler
President
Pharmaceutical
Manufacturers
Association



"Too many doctors are indifferent to the economic consequences of their decisions." So stated a recent issue of *Medical News Report* (December 4, 1972), an independent weekly newsletter published by former AMA Chief Executive F. J. L. Blasingame, M.D.

Doctor, are you indifferent...?

In discussing an anticipated increase in Blue Shield rates, Dr. Blasingame's newsletter had this to say:

"In general, it can be said, MD's have given the impression they are not particularly concerned with the increase in cost of health care to their patients...

"True, an MD's training is primarily scientific, but in the real world of practice, all of his scientific decisions have a price tag, or an economic impact. The economics of health care beckon the practitioner's attention. Concern for economics of medicine

When the pharmacist recommends that a drug product other than the one ordered be dispensed, the prescriber invariably permits the change when he feels the best interests of the patient will be served.

Shortcomings of Pro-Substitution Argument

The fact remains that it is necessary for the prescriber to know that the change is being contemplated, and to be in a position to consent or demur. Without that opportunity, the unilateral decision of the pharmacist made in the absence of clinical knowledge of the patient, could expose him to needless risks, and in addition, jeopardize the relationship between the professions of Pharmacy and Medicine. In my view, there is nothing in the pro-substitution argument that offsets these risks.

The Issue of Drug Knowledge

Substitution advocates claim that the primary justification for changing the rules is the desire to better utilize pharmacists' knowledge about drugs. Yet the pharmacist's task to keep current on the entire field of drug therapy, to some degree puts him at a disadvantage. Most often, a practicing physician will need expert knowledge of no more than 25

ould be an obligation of medical practice...

"Medical societies ought to conduct continuing campaigns to point out the substantial savings that could be realized thru deductible insurance and protection for catastrophic illnesses. At the very least, they should, in the patients' interest, question the statistics of any insurance organization that raises health care costs by forcing policyholders to buy insurance they may not need or want and probably won't ever use.

"Too many doctors are indifferent to the economic consequences of their decisions. Too many, for example, habitually hospitalize patients for the convenience of the MD. It's nonsense to deny such habits exist...

"Doctors, thru their medical societies, have unhesitatingly appealed to their patients for support in the fight against government interference with the private practice of medicine. And the public in the past has responded. It's time the American Medical Association and state and local medical societies paid off the debt by decisive action to hold down the cost of medical care."

Cost of Drugs

Insurance rates and hospital charges are only two factors in health

care costs. The cost of drugs—both prescription and nonprescription—is another.

And when it comes to drug costs, the nation's pharmacists are concerned. Through their national professional society, the American Pharmaceutical Association, pharmacists are advising the public to use nonprescription medication cautiously and conservatively, and to seek the advice of their pharmacist before selecting or purchasing such drugs.

Outdated Laws

The pharmacist also is aware that when it comes to prescription drugs, often he has an even greater opportunity to reduce the cost to the patient—with no sacrifice in the quality of the medication dispensed. But in many states, outdated and antiquated laws prevent the pharmacist from engaging in drug product selection. "Drug product selection" simply means that the pharmacist functions in the patient's interest by consciously choosing, from the multiple brands available, a low-cost quality brand of the specific drug to be dispensed in response to the physician's prescription order.

Much *misinformation* has been purposely spread by those who stand to gain financially by maintaining

the opposite.

Many pharmacists understandably are concerned about the cost of maintaining multiple stocks of similar products. While there is no doubt that inventory costs rise when additional brands are stocked, it would be interesting to know how much they rise, and how many pharmacists actually stock *all* brands—of, say, ampicillin or tetracycline—or how long they keep "slow moving" products on their shelves before they are returned for credit. To ask that the industry eliminate multiple sources is to ask competitors to stop competing.

Drug Substitution—A License for the Unethical

Anti-substitution repeal would favor "corner cutting" pharmacists and manufacturers. For them, free substitution would be not a right, but a license. As an aftermath, it is quite likely that the confidence of both physicians and patients in the profession of Pharmacy would be eroded, as revelations about the unconscionable behavior of an undisciplined few were magnified in the press or in professional circles.

Summary

In short, what the American Pharmaceutical Association advo-

high drug costs to the public. An endless stream of propaganda has emanated from the drug industry in an effort to persuade the medical profession that these so-called anti-substitution laws should be retained. And as long as these laws are retained, the drug industry will continue its current marketing practices which contribute unnecessarily to high drug costs to patients. These practices also are inviting government agencies to expand their restrictive controls on physicians and pharmacists.

APhA Efforts

As pharmacists, we are concerned about health care costs. We hope that every physician shares our concern on this vital issue, and will give his personal support to the constructive efforts APhA has undertaken in the interest of all patients.

(For a complete discussion of drug product selection, you are invited to request a free copy of the "White Paper on the Pharmacist's Role in Product Selection" from: American Pharmaceutical Association, 2215 Constitution Avenue, N.W., Washington, D.C. 20037.)

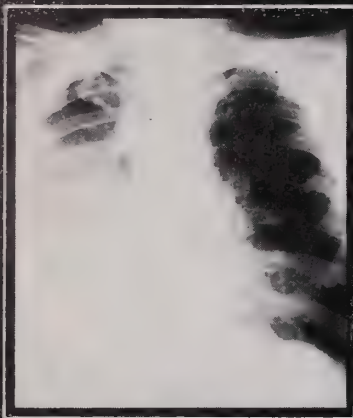
cates as a broad-spectrum panacea looks to us to be not only a minority view (advocacy of substitution is by no means a uniform policy in Pharmacy), but also an extraordinarily costly and ineffective remedy, whose side effects are odious. We believe (1) that an impressive majority of pharmacists prefer to work with Medicine and with industry, for the consumer, and for the general good, (2) that they seek the privilege to substitute when the patient might gain and when the patient's doctor agrees, and (3) that they seek to work for the resolution of genuine grievances openly and professionally.

(For amplification of PMA views, please write for our booklet, "The Medications Physicians Prescribe: Who Shall Determine the Source?" It is available from: Pharmaceutical Manufacturers Association, 1155 Fifteenth Street, N.W., Washington, D.C. 20005.)

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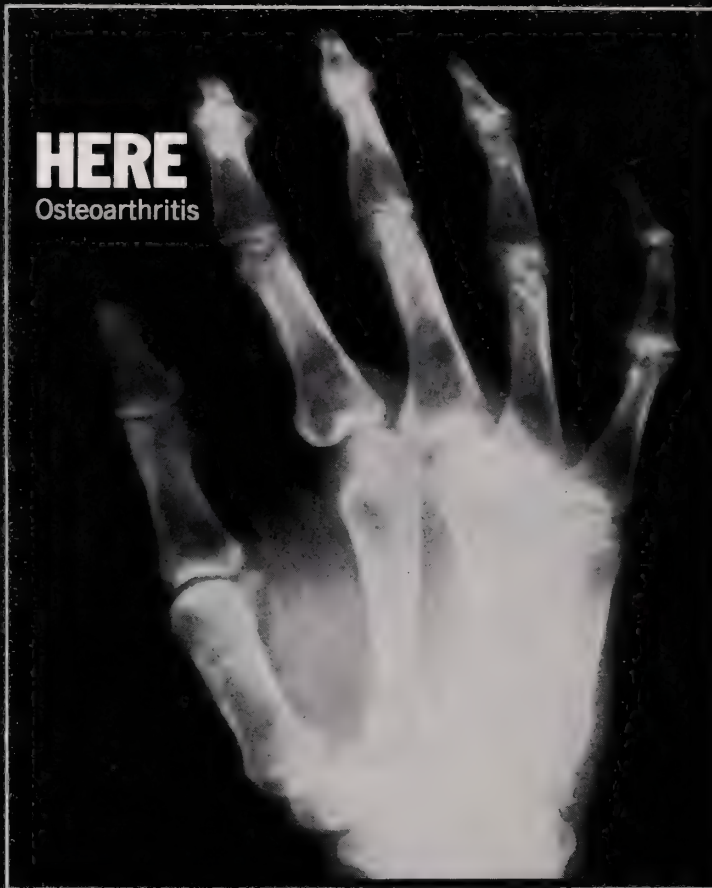


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COMITE CIENTIFICO

ABSTRACTOS

El Comité Científico invita a enviar abstractos de trabajo originales para considerarse para la Asamblea Anual que se llevará a efecto del 7 al 10 de noviembre de 1973, en el Hotel San Juan.

FECHA LIMITE PARA SOMETER ABSTRACTOS: JULIO 15, 1973

PARA MAS INFORMACION FAVOR DE COMUNICARSE CON EL
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José M. Rigau, MD
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PRECAUTIONS

May prove irritating to sensitized skin in rare cases. If this occurs, discontinue therapy. May stain.

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May interfere with thyroid function tests. Wait at least one month after discontinuance of therapy before performing these tests. The ferric chloride test for phenylketonuria (PKU) can yield a false-positive result if Vioform is present in the diaper or urine.

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Apply a thin layer to affected areas 3 or 4 times daily.

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Cream, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearyl alcohol, spermaceti, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of 5 and 20 Gm. **Ointment**, 3% iodochlorhydroxyquin and 1% hydrocortisone in a petrolatum base; tubes of 5 and 20 Gm. **Lotion**, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearic acid, cetyl alcohol, lanolin, propylene glycol, sorbitan trioleate, polysorbate 60, triethanolamine, methylparaben, propylparaben, and perfume Flora in water; plastic squeeze bottles of 15 ml. **Mild Cream**, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a water-washable base containing stearyl alcohol, spermaceti, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of ½ and 1 ounce. **Mild Ointment**, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a petrolatum base; tubes of ½ and 1 ounce.

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EMERGENCY MEDICAL CARE AND TRAFFIC FATALITIES IN PUERTO RICO

Stephan H. Fromm, MD, FACS
Gustavo A. Escalera, MD

In February 1971 the Puerto Rico Highway Safety Commission (1) noted that substandard and ill equipped ambulances, which lacked radio-communication and were driven by unqualified personnel, were taking traffic victims to emergency facilities which lacked equipment and personnel and which were giving inadequate service. That same year there were 42,577 traffic accidents causing 54,521 injuries of which 6,103 required hospitalization and 561 died. The purpose of this study is to determine how many of these traffic fatalities might have been prevented if adequate first aid and emergency medical care had been immediately available.

Method

The autopsy protocols of 531 of the 561 fatalities from traffic accidents in Puerto Rico during 1971 were reviewed. Eleven of the cases were eliminated from the study because of insufficient information to judge the severity of the injuries or the cause of death. The remaining 520 cases were evaluated and in each case an estimate was made of the victim's probable chances of survival if optimal emergency care had been immediately available, using the criteria described by Waller (2) in 1964.

An injury with a hospital death rate of less than 25 percent would classify the injury as probably salvageable, while a death rate over 75 percent would classify the injury as non-salvageable. All doubtful cases in this study were classified as non-salvageable. Some illustrative cases in the salvageable group will be presented below.

The accidents were considered urban if they occurred within greater metropolitan San Juan (including Bayamón, Carolina and Guaynabo) or within the city or town limits of the other municipalities. All other locations were considered rural.

Case Reports:

(10-11831) 21 year old man had an accident at 3 am on Jan. 16, 1971 in Old San Juan. He was taken to the Stop 19 Dispensary and from there sent to the Medical Center where he died a short time after arrival.

Autopsy revealed the cause of death as hemorrhagic shock from a ruptured spleen.

(10-12295) 48 year old man crashed his car against a pole at 1:30 am on July 3, 1971 in Hato Rey. He was taken to the Medical Center half an hour later, where he died

less than an hour later.

Autopsy revealed the cause of death as hemorrhagic shock due to external bleeding from a severely lacerated gluteal region.

(11-12537) 52 year old man crashed his car into a tree at 3 am on Dec. 24, 1971 in Cataño. He was taken by Police to the local Health Center, from where he was referred to the Medical Center about 9:00 am. Because he was unconscious and had anisocoria cerebral angiograms were performed and reported as negative. He died at 6 pm.

Autopsy revealed large hemoperitonum from a severely lacerated right kidney and death apparently due to hemorrhagic shock.

(16-01588) 48 year old woman was hit by a car at 7 am on August 3, 1971 in Patillas. She was taken by ambulance to the District Hospital, from where she was referred to the local Health Center, who sent her home. She was found dead in her home the next morning.

Autopsy revealed the cause of death as hemorrhagic shock due to a large retroperitoneal hemorrhage from a severely fractured pelvis.

(15-01259) 26 year old man was injured in a car accident in Adjuntas at 10:30 pm on December 24, 1971. He was seen at the Health Center that evening and sent home. He was again seen at the Health Center on Dec. 29, 1971, and again sent home. He returned very ill on Jan. 1, 1972 and died on the way to the District Hospital.

Autopsy revealed acute pulmonary edema and acute bilateral renal cortical necrosis. There was a large retroperitoneal hematoma from a fracture of the pelvis. The cause of death was felt to be acute renal failure producing heart failure caused by hemorrhagic shock.

(17-01784) 55 year old man crashed his car at 9 pm on May 24, 1971 on a rural portion of Highway No. 2. He was hospitalized at the District Hospital where he received supportive care until he died of "pneumonia" on May 26, 1971.

Autopsy revealed the cause of death to be severe respiratory insufficiency due to complete atelectasis of the left lung because of a large acute left diaphragmatic hernia.

The next case is presented as an illustration of a case classified as not-salvageable because of the combination of injuries even though it was felt that the type and severity of the lesions would not necessarily be fatal.

(14-04587) 55 year old man was hit by a car in Gurabo. He was found unconscious at the side of the road an undetermined time later, and taken to the local Health Center and from there sent to the Caguas Sub-Regional

Hospital. Because he remained unconscious and was found to have a fracture of the mandible he was sent to the Medical Center, but without any respiratory or circulatory support. He was dead on arrival at the Medical Center. Autopsy revealed a small subdural hematoma, fractured mandible, hemopneumothorax and hemoperitoneum from a lacerated spleen.

Results

A review of the 520 traffic fatalities revealed that 36 percent would have been salvageable if adequate emergency care would have been immediately available. It was found that 25 percent of the fatalities "died instantly" or were found dead. Five times more victims were found dead in rural areas than in urban ones, but only one of the urban ones was considered salvageable whereas 32 (30 percent) were considered so in the rural accidents. Among the victims found alive there was no difference in salvageability between urban and rural fatalities, suggesting that care is equally inadequate in all settings.

TABLE I: PLACE OF ACCIDENT

Found Dead (128)	Found Alive (392)
Urban (20) - 1 salvageable (5 percent)	Urban (141) - 52 salvageable (37 percent)
Rural (108) - 32 salvageable (30 percent)	Rural (251) - 98 salvageable (39 percent)

Table II shows the number of victims in relationship to the time of the accident. As might be expected many more salvageable injuries occurred in victims found dead at night or on week-ends than during daylight on week days. A higher percentage of salvageable injuries also obtained among the group found alive after 6 pm and week-ends, but this difference was not statistically significant.

TABLE II: TIME OF ACCIDENT

Found dead (128)	Found Alive (392)
Mon.-Fri. (6am - 6pm) 30 (5 salv. = 17 percent)	103 (32 salv. = 31 percent)
Eve and Weekends 98 (30 salv. = 30 percent)	289 (118 salv. = 41 percent)

Over 75 percent of the 392 victims found alive died in the first 24 hours after the accident, and over 45 percent of these were felt to be salvageable (Table III), whereas only 20 percent of those surviving over 24 hours were considered salvageable. Errors in diagnosis were the most common cause of delayed death in the salvageable group.

TABLE III: SURVIVAL TIME OF THE 392 VICTIMS FOUND ALIVE

	24 hours	Over 24 hours
Urban (141)	107 (47 salv.)	34 (5 salv.)
Rural (251)	201 (87 salv.)	50 (11 salv.)
	308 (134 salv. = 45 percent)	84 (11 salv. = 20 percent)

The type of injury responsible for death is presented in Table IV. More people died of hemorrhage or respiratory problems than of cerebral injuries, the latter being the cause of death in over 50 percent of traffic fatalities studied elsewhere. With prompt and adequate ventilatory support and volume replacement 67 percent of these 193 victims might have been saved. All major cardiovascular injuries, such as rupture of the heart or aorta, were considered not salvageable in this study.

TABLE IV: CAUSE OF DEATH IN 392 VICTIMS FOUND ALIVE

	Salvageable	Not Salvageable	Delayed
Cerebral (147)	9	98	40
Cervical (33)	7	24	2
Hemorrhage (149)	98	43	8 (4 salv.)
	67 percent		
Respiratory (44)	19	4	21 (8 salv.)
Infection (12)	1	---	11 (4 salv.)
Burns (6)	-	5	1
	392	134	174
			82

Conclusions

The fatality rate for traffic accidents in Puerto Rico in 1971 was 9.2 percent of those injured and hospitalized, which is well above the national average

of just under 3 percent (3). Frey (4) studied 159 traffic fatalities in Michigan during the period 1964-69 and estimated that 18 percent would have been salvaged if adequate care had been given immediately. Our salvage rate of 36 percent did not include some victims that might have been included as salvageable in other studies.

The number of salvageable victims among those found dead in rural areas, and the many who die in the first 24 hours indicates the magnitude of the problem we face. It is not enough to only improve the care received once the victim arrives at the medical facility, but the early recognition that an accident has occurred and the ability to respond promptly and effectively with first aid, resuscitation and rapid evacuation to the right medical facility are what will allow a decrease in this tragic death toll.

Waller (2) estimated that rural accidents carried 2.5 times greater mortality than similar urban ones in a study of 1960 accidents in California. We were unable to show any difference between rural and urban accidents in Puerto Rico, once the patient was found alive, indicating that the care received was apparently no different regardless of the area. That 50 percent of the fatalities were due to hemorrhage or respiratory problems, of which 67 percent were considered salvageable, indicates that any improvement in the delivery of emergency care should result in an early payoff of decreasing the case fatality rate.

Recommendations

1. Establish a committee or council on Emergency Medical Services at the Executive level, to study, design and implement a system of emergency care in which notification of an accident would rapidly dispatch an ambulance to the scene carrying personnel trained to aid those who now die from hemorrhage, anoxia, shock and spinal injuries. Under constant radiocommunication monitoring the victims could be triaged and evacuated to the facility best able to manage his injuries.

2. Emergency facilities need to be upgraded, organized, categorized and regionalized, so that adequate care is readily available.

3. Establish Trauma Centers where the highly specia-

lized care that some of these victims need could be concentrated.

4. Intercommunication (by radio) of all services involved in emergency work (police, civil defense, fire department, etc.).

5. Create a Trauma Registry in order to study the nature of accidents and the causes of death and disability.

6. Postgraduate education of all emergency room personnel.

7. Continued Medical Education on Trauma Care.

8. Education of the public in first aid and resuscitation.

Summary

During 1971 there were 561 traffic fatalities in Puerto Rico. Review of the autopsy protocols of 520 of these victims determined that 183 (36 percent) could have been saved if optimal emergency care had been immediately available. The majority of the salvageable victims died of hemorrhage or respiratory obstruction. There was no apparent difference in survival between rural and urban accidents. Recommendations on how to decrease this tragic toll are discussed.

Resumen

Durante 1971 en Puerto Rico murieron 561 personas en accidentes de tránsito. La revisión de 520 protocolos de autopsia de entre estas víctimas demostró que 183 (36 por ciento) pudieron haberse salvado si tratamiento de emergencia óptimo hubiese sido aplicado inmediatamente. La mayoría murieron de hemorragia y obstrucción respiratoria. No se encontró diferencia entre accidentes urbanos y rurales. Se discuten recomendaciones para mejorar los servicios de emergencia.

References

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2. Waller, *et al*: Calif. Med. 101: 272 (1964).
3. National Safety Council: Accidents Facts (1964).
4. Frey - J. Trauma: (1969)

INTRACRANIAL ANEURYSM SURGERY AT PUERTO RICO MEDICAL CENTER: OPERATIVE MORTALITY AND MORBIDITY

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José A. Alvarez de Choudens, MD
Nathan Rifkinson, MD
Pedro J. Borrás, MD
Bosto F. Martín, MD
Hiram Mercado, MD

Surgery for intracranial aneurysms is a relatively new undertaking, yet great advances have been made in reducing mortality and morbidity in these procedures. This is particularly so during the past few years with the advent of bipolar cautery and the use of the operating microscope as well as refinement in surgical skills.

The purpose of this communication is to show the results we have been obtaining at the Centro Médico with the hope that this will motivate physicians to refer these patients early and with a more optimistic outlook.

Between June 1970 and October 1972, 28 consecutive patients were operated upon, but only 26 are reported since two records were lost and detailed data could not be obtained in these two. We do know that one of them died, and is included in the mortality figures.

Age and Sex Incidence

In figure 1 we observe that none of these patients were children and that many cases fell in the 40 to 60 year-old group, which is generally accepted as the peak incidence of rupture of intracranial aneurysms. Though it is generally accepted that this is a congenital disease, it is interesting to note that they usually do not become symptomatic until adult life and many times in late adult years.

In this particular study females were affected considerably more than males, though we do not think this of significance.

Vessel Site

Figure 2 shows that among our cases, aneurysms were noticed to be much more common in the internal carotid artery at the site where the posterior communicating artery originates. We see that anterior communicating

AGE INCIDENCE

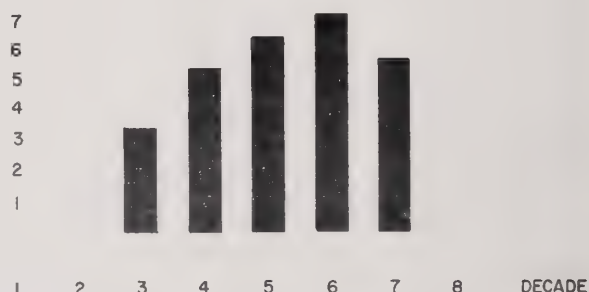


FIGURE 1

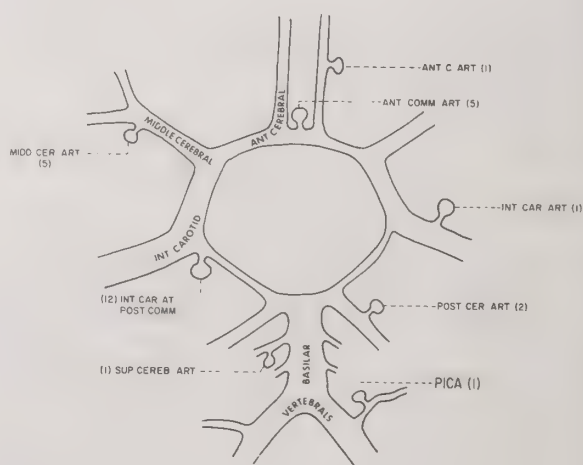


FIGURE 2. GRAPHIC ILLUSTRATION OF ANEURYSMAL SITES.

ing and middle cerebral aneurysms were also relatively common. Many studies have shown equal frequency for these three sites; some have shown anterior communicating aneurysms more frequent than the rest. Aneurysms in the posterior fossa of the head are relatively uncommon.

Presenting Signs and Symptoms

Most of the aneurysms presented with subarachnoid hemorrhage. Many of these hemorrhages were not associated with any neurological signs or symptoms, but a few were accompanied by hemiparesis, ocular weaknesses, or other signs. Three patients presented with just extraocular muscle weakness, usually a third nerve palsy, and two patients presented with sudden headaches in which a subarachnoid hemorrhage was not verified.

Type of Operation

Almost all these aneurysms were treated by primary exclusion from the circulation; that is, ligation of their neck by either clip or ligature or by ligating its parent vessel, proximally and distal to the aneurysm. In one of the aneurysms, only one main feeder was ligated and in another, reenforcement of the walls of the aneurysm by placing gauze around it was done, as no other means of obliterating it was found feasible.

Classification of Patients, According to Operative Risk

In order to evaluate the results of aneurysm surgery, one must consider the patient's condition immediately before the operation. Usually the better the condition of the patient, the better are the operative results, both in terms of mortality and morbidity. A classification has been devised and accepted world-wide in which these cases are divided into Grades I to IV.

A Grade I patient is one that just before operation is completely normal both as far as symptoms and signs, except perhaps may complain of mild headache or may have mild nuchal resistance.

A Grade II patient is one with moderate headache and stiff neck but who exhibits no neurologic deficit, other than a paralysis of ocular movements. Both Grade I and II patients must be alert and mentally clear to qualify for this classification.

In Grade III, the patient has an altered level of consciousness, either being lethargic or semi-stuporous or having mental confusion. Patients who have major neurologic deficit like a hemiparesis, also fall into this category.

In Grade IV, the patient is comatose or semi-comatose.

Results

27 cases were operated, 25 of which were in categories, I and II and 2 were Grade III, just prior to the operation. Of the 25 good risk patients only 1 died, while 1 of the 2 bad risk patients died. This does not include a patient that was Grade I who died much later, but from a second aneurysm, not from the one that was surgically treated. These results can be seen graphically in Table I.

TABLE I: MORTALITY AS RELATED TO OPERATIVE RISK

Grades I and 2	1 of 25 cases — 4 percent
Grade 3	1 of 2 cases — 50 percent
Grade 4	None operated at this level
One patient died months later from a second aneurysm after succesful operation for the first.	

Quality of Survival

Perhaps as important as the mortality figures are the morbidity figures. It would be useless to operate on these patients if they are to remain incapacitated. Again, we divide the patients in 2 groups, according to risk.

Table II shows that of all the patients operated who were good candidates, none remained totally incapacitated. Six were partially incapacitated and 18 recovered. The sole survival of the Grade III group remained totally incapacitated. We must qualify that among the patients categorized as recovered, four of them were left with a weakness of eye movements on one side, but which did not interfere significantly with any of their activities.

Table III tells us the degree of disability among the patients that did not recover completely. As was mentioned, one patient of the entire group that survived was left completely disabled, having a right hemiparesis and severe intellectual changes. Of all the cases that were partially disabled, we can see that the degree of disability was of such nature that the

TABLE II: QUALITY OF SURVIVAL

	Incapacitated		Recovered	
	Total	Partial		
Gr. 1, 2	0	6	18	(24)
Gr. 3	1	0	0	(1)

Four in the recovered group were left with non disabling ocular palsies.

TABLE III: DEGREE OF DISABILITY

- 1) Severe: one case
Rt. hemiparesis, severe
intellectual changes.
- 2) Not severe: six cases
Two with mild dist. of memory
(one of these also had dysarthria)

Two with mild to moderate paresis (one
of these also controlled epilepsy)

Two with mild dysphasia (one also
moderate hemiparesis)

patients could still take care of themselves and were able to function to a considerable degree, even including employment in some of them.

Interval Between Clinical Manifestations and Operation

Another factor we would like to consider is the interval between the onset of symptoms of hemorrhage and the time when the patient was operated. It is thought that the longer one waits and lets the patient recover

from the original insult, the better the results will be. Yet, from this limited study we observe that we had no worse mortality or morbidity operating these patients within the first two weeks of illness than when the group is considered as a whole. In general, what we do with these patients is to wait at least 3 to 4 days after the hemorrhage or until the patient improves to a Grade I or II condition if his original state was worse than that. Once they reach this level, we try to operate them as soon as possible.

Discussion

Summarizing, we can see that of all the good risk patients we had bad results in only one of 25 patients; the rest of them recovered or were left with disabilities which did not interfere with self care or, in most instances, with employment. Of the bad risk patients, the two of them had bad results. It follows that we should not operate on grade III or IV cases. If we compare results with other series (Table IV) we see that our results are at least as good as the latest figures that could be found in the world literature and perhaps better than in many places.

What happens if you just leave these patients alone and not operate them? This has always been very controversial. The best data, comes from the Cooperative Study of Intracranial Aneurysms and Subarachnoid Hemorrhages, in which 20 institutions participated bet-

TABLE IV: COMPARATIVE RESULTS

Present series	4 percent
Cooperative study of IC aneurysms and SAH	20 percent
Hunt and Hess, Ohio St. Univ., 1968	14 percent
Paul and Arnold, U. of Md., '70	19 percent
Norlen, Sweden, 1958-64	0 percent

ween the United States and England, in 1966. From this data, it was felt that once an aneurysm ruptures or becomes symptomatic the chances of death within one year, ranges from 40 percent to 90 percent. If we just take the lower limits, even that is quite frightening, and in our opinion, justifies the surgical approach to this disease whenever possible.

Summary

We have presented mortality and morbidity results of 27 patients operated on for symptomatic intracranial aneurysms.

Two patients that were operated while in bad condition (Grade III & IV) yielded bad results, manifested by either death or severe disability. In good risk cases there was only a 4 percent mortality, and among those who lived, none were left with severely incapacitating deficits. Eighteen of 24 were considered to have recovered completely.

Resumen

La mortalidad y morbilidad de 27 pacientes operados por aneurismas intracraniales sintomáticos se ha presen-

tado. Dos pacientes fueron operados en condiciones pobres obteniendo malos resultados, manifestados por muerte o incapacidad severa. En pacientes en buenas condiciones tenemos una mortalidad de 4 por ciento y ninguno de los supervivientes quedó con incapacidad severa. Dieciocho de 24 pacientes recuperaron por completo.

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SEASONAL PATTERN OF BIRTHS IN PUERTO RICO

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Abelardo Fuertes de la Haba, MD, DPH, FACOG

It has been said that man is the only creature who eats when he is not hungry, drinks when he is not thirsty and makes love all the time. If the last of these three characteristics referred to about man were true, one would expect that during, say, a period of one year, the results of this behavior of love-making in terms of births would be an uniformly distributed probabilistic phenomenon. However, when the data of births are studied over a certain period of time, there are deviations noted. These deviations in case of births, during the calendar year of 12 months, are markedly different from month to month. When this monthly phenomenon is observed from year to year, there is seen to be a certain fixed pattern in monthly distribution. Does this pattern show any seasonal variation? If it does, man, just like other creatures on this earth, may be following the seasonal conception pattern. Knowing, however, the superiority of man's intellectual capacity, one would attribute this seasonal pattern of conception to the traditional activities for customs which are in turn determined according to the season of the year.

To have an illustration of this pattern, the percent distribution of yearly births by month in the United States from year 1950 to 1961 is shown in Table I, and Graph 1. The months of August (9.04 percent) and September (8.92 percent) are the ones having, on an average, the highest percent of the births during this period under study. The percent goes down later during the year and fluctuates at a lower level during the months from January to April and starts rising again. If one studies such a pattern and tries to fit a cyclic equation, it is possible to arrive at logical and meaningful implications explaining the seasonal phenomenon. In this paper, the authors have made an attempt to present the preliminary overall analysis of the births

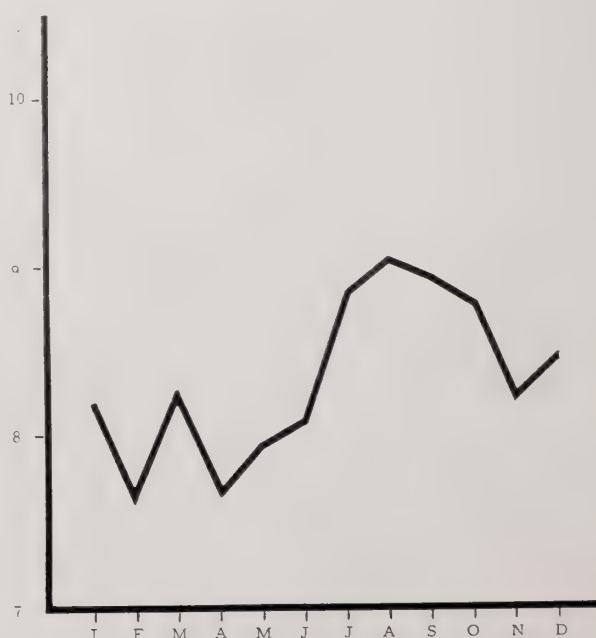
pattern in Puerto Rico over a period of 22 years, from 1950 to 1971.

Annual Births in Puerto Rico

In year 1960, the registered births in Puerto Rico amounted to slightly over 85,000 (Graph 2). The total of births has been decreasing slowly and except for a few upward values, has been around 70,000 in the last four years. The birth rate in Puerto Rico has been on the decline, from 38.5 in 1950 to 25.6 in 1971. (Rates per 1,000 population).

GRAPH 1

Average Percent Distribution of Births, U.S.A., 1950 - 61



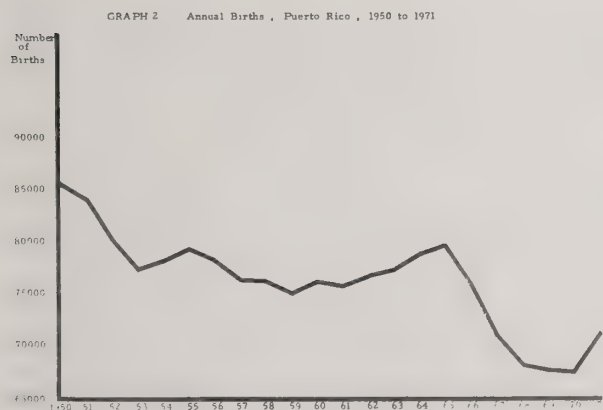
From the College of Education, and Department of Obstetrics and Gynecology of the Maternal Health Program, at the School of Medicine, UPR.

Presented at the American Statistical Association, Social Statistic Section, Montreal, Canada, August 14, 1972.

TABLE 1: AVERAGE PERCENT DISTRIBUTION OF BIRTHS, U. S. A., 1950-1961

Month	Average Births (Percent)
January	8.19
February	7.63
March	8.26
April	7.64
May	7.95
June	8.09
July	8.84
August	9.04
September	8.92
October	8.76
November	8.21
December	8.47
Total	100.00

Source of information: The average percent is evaluated from the original data taken from Register life birth in the United States of America "Vital Statistics of U. S. A. year 1961 Vol I, page 1-28.



Monthly Percentage Distribution

The pattern of monthly births within the year, however, has a peculiar form. In order to be able to compare such pattern from year to year the registered births by months are distributed as percentage of the yearly total.

Table II and Graph 3, show these percentages. Deviations of the monthly percentage from the expected value 8.33 percent can be seen to be markedly similar since 1954 to 1969. It may be noted that the propor-

tion of births increase from July until October and starts declining during the next four months, whereafter the births stay fluctuative at the same low level for the next four months. There are such three distinct seasonal periods in the year. Table III and Graph 4 show the average trend of these percentages over a period of 22 years. The figures indicate three distinct seasonal periods of the year, namely July to October: Increase. November to February: Decline. March to June: Fluctuating at a low level.

Interpretation of the Pattern

In order to interpret the birth pattern, one would go back to the possible time of conception. The normal time of 9 months and 10 days places the highest conception period in relation to the above dates, between October and January, the winter time and the lowest one between May and August, the summer time. The winter time generally keeps people more at home with less outdoor activities. Besides it includes several long periods of social festivities such as Christmas. In Puerto Rico Christmas celebrations generally start almost at the beginning of December and lasts until the first half of January of next year. The summer time is spent more outdoors due to vacation time for children and also adults. These activities accompanied by less privacy may induce low frequency of love-making opportunities and hence of conception compared with the winter time's privacy and the reaction in the mood during and after the festive days of Christmas time.

Fitting a Cyclic Curve

The pattern is such a regular one, at least for the data on hand, that it was decided to determine the equation for this seasonal phenomenon. A sine-cosine curve was tried to fit to the average percentages. The curve fitted turned out to be as follows:

$$Y = 8.33 - 0.6025 \sin (30X)^{\circ} + 0.2439 \cos (30 X)^{\circ}$$

where Y = percent monthly births

and X = coded number of month (January = 1, December = 12)

The fit is highly significant (Prob. level 1 percent), 75.2 percent of the variation explained by the time variable, X.

The maximum value of Y occurs at X = 9.7 months. If one considers the middle of the month as the point of coincidence for the coded number, this maximum

TABLE II: PERCENTAGE DISTRIBUTION OF BIRTHS BY MONTH, PUERTO RICO, FROM 1950
TO 1971

	1950	1951	1952	1953	1954	1955	1956	1957	1958	1959	1960	1961	1962	1963	1964	1965	1966	1967	1968	1969	1970	1971
January	8.77	8.61	7.79	8.19	8.00	8.51	8.56	8.68	8.26	8.38	8.54	8.42	8.02	8.22	8.28	8.32	8.74	8.58	8.31	8.38	8.05	8.80
February	7.85	7.51	7.09	6.87	7.40	7.29	7.91	7.52	7.40	7.35	7.60	7.38	7.20	7.18	7.47	7.36	7.76	7.14	7.45	7.46	6.82	7.74
March	8.52	8.44	8.39	7.71	7.99	7.88	8.17	8.23	8.02	7.64	7.74	7.88	8.01	7.91	8.04	8.12	8.11	8.22	7.91	8.06	7.45	7.98
April	8.62	8.48	8.64	8.25	7.61	8.01	7.61	7.77	7.71	7.69	7.76	7.53	7.79	7.60	7.58	7.60	7.74	8.11	7.49	7.76	7.34	7.84
May	8.62	8.79	8.99	8.49	8.20	8.29	7.81	7.58	7.78	7.90	8.06	7.98	8.05	8.03	7.68	7.87	8.15	8.11	8.28	7.98	7.93	7.76
June	8.00	8.12	8.18	8.33	7.87	8.03	7.70	7.64	7.07	7.55	7.62	7.77	7.72	7.85	7.31	7.63	7.77	7.94	7.69	7.55	7.07	7.76
July	8.22	8.47	8.23	8.59	8.29	8.47	8.10	8.19	7.99	7.99	8.26	8.39	8.26	8.29	7.56	8.29	8.04	8.22	8.37	8.01	7.85	8.12
August	8.11	8.56	8.69	8.79	8.80	8.75	8.75	8.83	8.82	8.89	8.89	8.61	8.89	8.67	8.62	8.71	8.57	8.76	8.38	8.51	8.67	8.47
September	8.55	8.72	8.85	8.96	9.19	8.96	9.21	9.47	9.54	9.49	9.34	9.42	9.17	9.43	9.42	9.47	9.15	9.26	9.37	9.34	9.49	9.13
October	8.59	8.51	8.63	9.09	9.36	9.10	9.26	9.18	9.55	9.47	9.22	9.26	9.37	9.34	9.66	9.51	9.14	9.16	9.35	9.50	9.69	9.25
November	7.87	7.73	8.22	8.53	8.71	8.28	8.41	8.51	8.97	8.79	8.45	8.71	8.88	8.80	9.28	8.61	8.55	8.23	8.57	8.78	9.82	8.65
December	8.28	8.06	8.30	8.20	8.58	8.43	8.51	8.40	8.89	8.86	8.52	8.65	8.64	8.68	9.10	8.51	8.28	8.27	8.83	8.67	9.82	8.50
Total	100.00	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100
Total Births -	85455	84007	80200	77380	78008	79221	78177	76067	74933	76015	75563	76677	77382	78837	79586	75735	67989	67577	67438	71117		

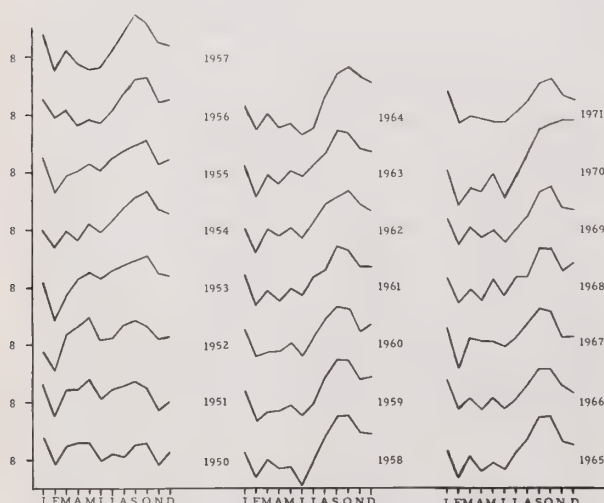
Source of information: The percentages have been computed from the original data compiled from the Puerto Rico Department of Health monthly and annual reports for the corresponding years, obtained from Mr. Luis Collazo of Division of Statistics of the Health Department.

TABLE III: AVERAGE PERCENT DISTRIBUTION OF BIRTHS OBSERVED AND ESTIMATED, PUERTO RICO, 1950-1971

Month	Average Births Observed (Percent)	Estimated Trend Value (Percent)
January	8.38	8.24
February	7.40	7.93
March	8.03	7.73
April	7.86	7.69
May	8.11	7.82
June	7.74	8.09
July	8.20	8.42
August	8.67	8.73
September	9.21	8.94
October	9.22	8.98
November	8.60	8.85
December	8.58	8.58
Total	100.00	100.00
Average Yearly Births (1950-1971)	76,100	76,100

GRAPH 3

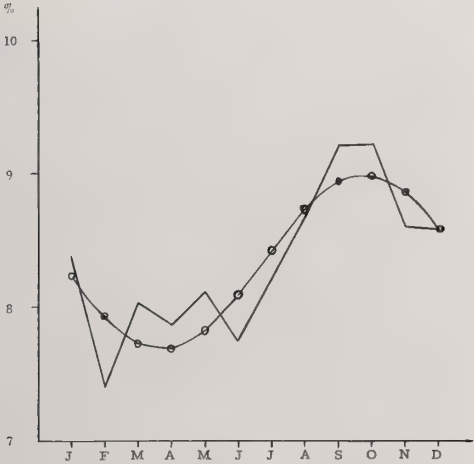
Percent Distribution of Monthly Births, Puerto Rico, 1950 to 1971



GRAPH 4

Average Percent of Yearly Births by Months (Data 1950 to 1971),
Puerto Rico

Observed %
Estimated %
Estimated Percent Birth for the Month = $8.333 - 0.6025 \text{ Sine } (30 X) + 0.2439 \text{ Cosine } (30 X)$
(X = Number of Month, January=1 December=12)



value would represent the first week of October as the peak point of birth, thus indicating roughly the Christmas time as the highest incidence of conception.

Some Implications of this Pattern

In a democratic society like the one we are living in, one cannot force to change the human behavior which does not interfere in the freedom of the other fellowman. Hence the society has to accept this and must try to meet with the demand it would create in terms of hospital beds, doctors and nurses for the peak delivery period.

On the other hand, the society which is planning

a birth control program, may have to carry out this propaganda campaign during this peak period of conception making people more conscious of this matter and may gain some impact on their control program. Anyway, man is supposed to have his own way of living, behaving and carrying on his personal activities as he wishes. However, he is born in a certain type of society with customs and traditions already prevailing from long time before he was born, and therefore, he, in general, is not as free as he thinks he is. He is influenced directly by this society that has customs and traditions which in turn are influenced by the climate and other natural surroundings. Thus, even if man is said to be a creature who makes love all the time, one would say, from the above data, that he may be following, indirectly, some pattern of seasonability of nature like other creatures.

Summary

“Man is the only creature who eats when he is not hungry, drinks when he is not thirsty and makes love all the time”. If the last of these three characteristics of man were true, we would, assuming other factors constant, expect that the result of this behavior of love-making in terms of births would be an uniformly distributed probabilistic phenomenon, say, over a year’s time. Which factors (natural as well as man-made) control or produce deviations in this pattern is a question still not studied for different countries or races. In this paper, an attempt is made to analyze monthly distribution of births and birth rates in Puerto Rico over a period of the last twenty years. A markedly seasonal pattern is observed throughout the period under study. A mathematical curve is fitted to the data and some sociological implications are discussed. A comparison is also made with United States data.

THE PAGET-VON SCHROETTER SYNDROME

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A case of "effort" thrombosis of the axillary vein treated at the Industrial Hospital of the Puerto Rico Medical Center is the basis for this report. Although this entity accounts for only a small percentage of all thrombophlebitic episodes seen, it is not, by any means, a rare condition and should always therefore be considered in the diagnosis of venous obstructive problems of the upper extremities.

Classically described by Paget in 1875, and again nine years later by von Schroetter, the Paget-von Schroetter Syndrome (Intermittent Venous Claudication of the Upper Extremity) has been the subject of thorough investigation, especially by German authors. Precisely this emphasis on exact interpretation of the etiology and pathology involved has led to some degree of confusion and differences of opinion among researchers, based perhaps on the existence of multiple etiologic factors.

Case Report (Figures 1, 2)

J. A. R. - a 37 y/o male was admitted on May 27, 1971 to the Industrial Hospital, with pain, congestion, and swelling of the right arm. Twelve days prior to admission the patient felt a sharp, lancinating pain in the right arm extending to the axilla, followed by diffuse swelling of the arm and hand. At the time, the patient was lifting a bucket full of cement.

The venous pattern over the anterior thorax became prominent. Physical examination was within normal limits except for marked swelling of the right arm and accentuated venous pattern over the thorax and upper arm (Fig. 1). Radial, ulnar, and brachial pulses were not diminished.

A venogram was performed, demonstrating almost complete obstruction of the subclavian vein with extensive collateral formation (Figure 2). Lung scanning was normal. Treated with intravenous Heparin, he improved and was discharged on June 18, 1971, except for occasional axillary discomfort.



Fig. 1: A view of the patient. Notice prominent swelling of arm and shoulder and accentuated venous pattern over thorax and upper arm.



Fig. 2: A venogram performed during hospitalization revealed obstruction of the subclavian vein and extensive collaterals.

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Discussion

Without question, there is growing awareness of the importance of all forms of venous thrombosis and its thromboembolic complications. Attention has been centered on the lower extremity and the right side of the heart as the primary site of lodgement for the threatening thrombus.

As industrialization proceeds in Puerto Rico and trauma assumes epidemic proportions, especially in a society not particularly oriented to prevention, a timely reminder of the potential importance of the upper extremity in these thrombotic problems is in order.

Review of the subject reveals the following:

1. Clinical features: (1, 2)

Males are more frequently affected than females. Peak age for effort thrombosis is between 20 and 29 years, although patients from age 11 to age 75 have been involved. Hughes (1) reported greater incidence of right sided pathology without relationship to the patient's right or left-handed tendencies.

About 11 percent of patients have immediate clinical manifestations, 37 percent within an hour, increasing to 87 percent within 24 hours. In the remainder, symptoms appear 24 hours after the precipitating effort.

The three chief symptoms which appear in almost all patients are swelling, pain and discoloration of the extremity (1). Most patients show marked edema, and not only is the entire extremity affected, but also the chest wall and neck. Vein distention becomes quite noticeable, as collaterals appear, and can be demonstrated readily by infra red venography (4). About one third of patients complain of pain, which may affect the whole arm or limit itself to the shoulder girdle. Discoloration of the extremity — it usually appears cyanotic from venous stasis — may also be red, pink or white. Other symptoms are varied, and at times vague: numbness, aching, stiffness, diffuse weakness, tenderness in the axilla, lightness, coldness, fever, pruritis, snapping sensation and easy fatigability.

2. Pathogenesis

At least fifteen precipitating factors have been mentioned in venous obstruction in the axillary and subclavian veins. In all of them, the "common denominator" seems to be severe effort, followed by damage to the vessel wall with or without thrombus formation in the roughened intima. The following can be so classified: sudden stretching and compression of the vein; rupture of the subclavian axillary valve under the subclavian muscle; damage to the endothelium by distention of the axillary vein resulting

from respiratory effort; injury to the intima as a result of pressure on the vein by the coracoid ligament and subclavian muscle with the arm extended and abducted; irritation of the perivenous sympathetic plexus resulting in vasospasm and thrombus formation; local venous spasm from stimulation of the sympathetic neurons as the end result of a reflex disorder; chemical changes in the blood due to catabolites of abnormal metabolism; constriction of the subclavian vein below the head of the humerus and against the subscapularis muscle in hyperabduction of the arm; hematoma in the axillary region, direct compression of the vein and even extravascular obstruction by the phrenic nerve.

Of the many motions described by patients are: throwing a ball, swimming, carrying of heavy buckets, pushing a heavy object, sudden flexion of the arm, a fall in the hand and holding of high-spirited animals.

3. Physical Examination

The most consistent findings are swelling of the arm due to non-pitting edema and increased venous pressure, evidenced by the engorged veins. Resting venous pressures of 21-41 cm H₂O have been reported by Hughes (1), as compared to normal pressures of 5-12 cm H₂O. Cyanosis, palpable venous cord, decreased temperature in the arm, tenderness of the affected vessel, and a sensation of fullness over the anterior chest are frequently observed.

Other less frequent findings include mottled skin, pitting edema, fever, rubor, weakness, induration, pallor on elevation, lymphadenopathy, dry skin, ecchymoses, congestion, and excessive sweating.

Special tests have proven useful in cases of obscure or difficult diagnosis. These include a prolonged circulation time, decreased O₂ saturation, no appreciable departure from normal arterial pressure, and no difference in cutaneous absorption of sodium chloride from the unaffected extremity. The utility of infra-red venography has already been mentioned.

Hematological tests present small changes such as a slight leukocytosis, and a slight increase in the sedimentation rate.

4. Differential Diagnosis

Several conditions should be considered in the differential diagnosis: namely cardiac failure; cervical ribs; axillary compression; thrombosis; complicating septic processes, gout, polycythemia vera; aneurysms; central or peripheral neuropathies; and mediastinal compression due to tumor or other causes. History is very important in establishing the diagnosis.

5. Complications

The threat of pulmonary embolism is less after

effort thrombosis than in other thrombotic conditions of the upper extremity because the primary injury to the wall is such that a thrombus quickly adheres to the damaged area (3). In addition high flow aids in preventing propagation. Nevertheless, morbidity may be sufficient to incapacitate the patient.

6. Treatment

Anticoagulants prove useful when administered as soon as possible after onset. Stellate sympathetic block has been advocated to diminish postulated venous spasm. Heat applications, arm elevation, and compression bandages have been tried. In some series, residual effects have been present in over 75 percent of the cases. This indicates the need of early treatment to reestablish venous return. Some authors have favored proximal ligation of the vessels, others, thrombectomy, and a few, venous bypass operations (5). Each case must be judged on an individual basis, and the decision based on venograms, onset of the disease, its course and accompanying injuries. Since our patient was referred twelve days after the initial episode, we chose conservative treatment, with good results.

Summary

Based on a case report, we have reviewed the pertinent observations on effort thrombosis of the axillary

subclavian vein, known as the Paget-von Schroetter Syndrome.

Resumen

Basados en la presentación de un caso, se discuten los aspectos más importantes del síndrome Paget-von Schroetter o trombosis al esfuerzo de la vena axilo-subclavia.

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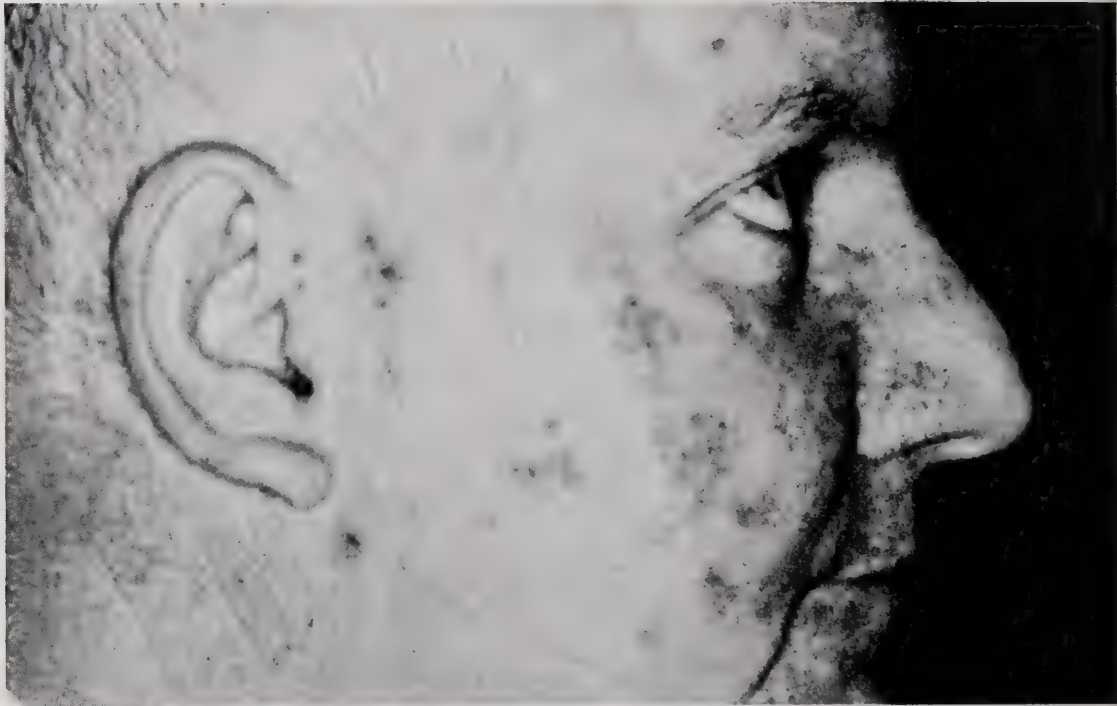
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What's on your patient's face...

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Patient P.T.* seen on 3/29/67 shows typical lesions of moderately severe keratoses. Note residual scarring on ridge of nose from previous cryosurgical and electrosurgical procedures.



Patient P.T.* seen on 6/12/67, seven weeks after discontinuation of 5% FU cream. Reaction has subsided. Residual scarring not seen except that due to prior surgery. Inflammation has cleared and face is clear of keratotic lesions.

*Data on file, Hoffmann-La Roche Inc., Nutley, N.J



**The lesions on his face
are solar/actinic—
so-called “senile” keratoses...
and they may be premalignant.**

Solar, actinic or senile keratoses

These lesions may be called by several names, but they usually can be identified by the following characteristics. The typical lesion is flat or slightly elevated, of a brownish or reddish color, papular, dry, rough, adherent and sharply defined. They commonly occur as multiple lesions, chiefly on the exposed portions of the skin.

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Before prescribing, please consult complete product information, a summary of which follows:

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Contraindications: Patients with known hypersensitivity to any of its components.

Warnings: If occlusive dressing used, may increase inflammatory reactions in adjacent normal skin. Avoid prolonged exposure to ultraviolet rays. Safe use in pregnancy not established.

Precautions: If applied with fingers, wash hands immediately. Apply with care near eyes, nose and mouth. Lesions failing to respond or recurring should be biopsied.

Adverse Reactions: Local—pain, pruritus, hyperpigmentation and burning at application site most frequent; also dermatitis, scarring, soreness and tenderness. Also reported—insomnia, stomatitis, suppuration, scaling, swelling, irritability, medicinal taste, photosensitivity, lacrimation, leukocytosis, thrombocytopenia, toxic granulation and eosinophilia.

Dosage and Administration: Apply sufficient quantity to cover lesion twice daily with nonmetal applicator or suitable glove. Usual duration of therapy is 2 to 4 weeks.

How Supplied: Solution, 10-ml drop dispensers—containing 2% or 5% fluorouracil on a weight/weight basis, compounded with propylene glycol, tris(hydroxymethyl)-aminomethane, hydroxypropyl cellulose, parabens (methyl and propyl) and disodium edetate.

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SUPERIOR VENA CAVA SYNDROME CAUSED BY A MALIGNANT THYMOMA — CASE REPORT

Alberto J. Larrieu, MD

Jorge O. Just Viera, MD

Since William Hunter's original description, obstruction of the superior vena cava (SVC) is known to produce characteristic signs and symptoms. Whereas, Hunter's patient had a syphilitic aneurysm of the thoracic aorta, this has become a rare cause of the superior vena cava syndrome. At present bronchogenic carcinoma is the most common etiology. We encountered a patient with an unusual cause of the syndrome, malignant thymoma, and wish to report it.

Case Report

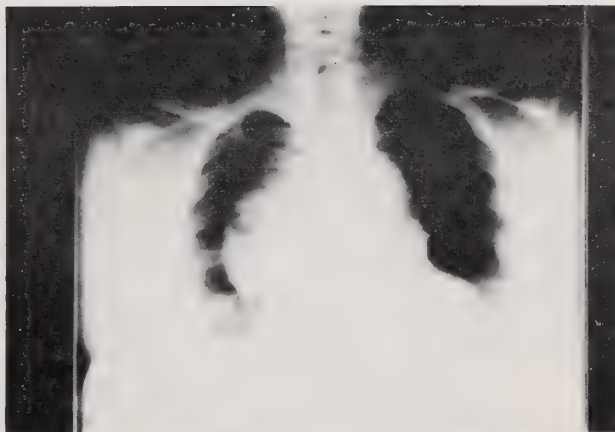
A 42-year old white female, was admitted to San Juan City Hospital on April 13, 1971 with prominent swelling of the face and upper extremities, six months in duration. She also complained of orthopnea and dyspnea on effort. Physical examination revealed a chronically ill female, plethora, engorged veins, cyanosis of the upper extremity and face, and marked swelling of the head and anterior chest.

Roentgenographic examination revealed a large mediastinal mass (Figures 1 and 2). Bronchoscopy and supraclavicular node biopsy, performed initially, did not yield a diagnosis. Direct biopsy of the mediastinal mass through the second right intercostal space revealed a malignant thymoma.

Because the tumor was extensive, invasive and unresectable, she received a 5 week radiotherapy course of 5000 rads with cobalt 60.

After radiotherapy, slight swelling of the face and dyspnea persisted. Chemotherapy, consisting of intravenous Cytosan, 15 mg/kg was administered accompanied by prednisone which was later discontinued. She experienced considerable symptomatic improvement, however, chest films revealed multiple lung metastases. Subsequently, she was maintained on 750 mg cytoxan intravenously every 2 weeks, without recurrence of superior vena cava obstruction.

On March 15, 1973 the patient underwent a biopsy of a hard mass inferior and anterior to the left lateral malleolus reported as an epidermoid carcinoma infiltrating the talus bone. After an extensive unproductive search for another malignancy it was considered to be metastatic from the previous tumor. At this time another metastatic lesion to the second lumbar vertebra was detected by roentgenograms and she was started on radiotherapy to this site two years after discovery of the initial mediastinal mass.



Figs. 1, 2: Roentgenograms of the chest demonstrating the large mediastinal mass which caused the superior vena cava syndrome in this patient.

From the Section of Thoracic Surgery, San Juan City Hospital and the University of Puerto Rico School of Medicine.

Discussion

Obstruction of the superior vena cava presents a clinical problem encompassing three stages: detection, diagnosis and treatment. Although the full blown clinical picture is obvious, the early stages are often disregarded, as in this case, or are confused with other conditions, such as angioneurotic edema, allergic blepharitis, or even congestive heart failure (1, 2).

Most common symptoms include headache, somnolence, respiratory distress, dizziness and visual disturbances, all of which are intensified by stooping or recumbence. The prominent signs include increased venous pressure, edema of the head, neck, arm and upper extremities; cyanosis of the upper half of the body and dilatation of the superficial veins of the upper extremity, head and neck (1, 2, 3, 4).

Lowenberg (3) has summarized some of the specific examinations which facilitate diagnosis in this condition:

1. Antecubital venous pressure readings
2. Venography and intravenous angiocardiology
3. A diagnostic chest work up:
 - a. standard X-rays examination of the chest
 - b. laminography
 - c. bronchoscopy, study of bronchial washings and lung biopsy.
 - d. scalenus node biopsy (this procedure may be quite bloody)
 - e. direct biopsy (needle in second intercostal space)
 - f. mediastinoscopy in selected cases.
4. Histoplasmosis and Tuberculosis Tests:
 - a. skin test
 - b. complement fixation test
 - c. culture of the organism from blood, sputum, bronchial secretions and bone marrow.
5. Test for luetic infection

Recent reports in the literature include four large series with a total of 218 cases (1, 5, 6, 7).

Failor et al (6), found at necropsy that 18 of 33 cases were due to bronchogenic carcinoma; all originated in the right lung, and penetrated the wall of the superior vena cava. Other causes were malignant lymphoma (15 percent) and chronic mediastinitis (12 percent). Only one case in the entire series was due to carcinoma of the thymus.

Similarly, Effler and Groves (1), found malignancy in 75 percent of their 64 patients; of these tumors, an overwhelming majority originated in the right lung particularly in the right upper lobe. In 1965, Hanlon

and Danis (5), reported on a group of 60 patients that included one patient with thymic sarcoma. Again, 75 percent of the superior vena cava obstructions resulted from tumor, specially from the right upper lobe of the lung. Urschel and Paulson (7), found 61 patients with this syndrome and 55 had a malignant neoplasm. None had a thymic tumor.

Thus, in these 218 cases, 85 percent had malignancies, and 75 percent had right sided bronchogenic carcinoma. In only 2 patients was the obstruction thymic in origin. An additional patient with malignant thymoma causing the superior vena cava syndrome was reported by Marshall et al (8), in 1967.

As contrast, in the extensive review published by McIntire and Sykes (9) in 1949, primary malignant thoracic tumors accounted for only 33 percent of their patients, aneurysms for 30 percent and chronic fibrous mediastinitis for 1.5 percent. Rare tumors accounted for 31 percent. Less common, even rare causes, are histoplasmosis (3, 7, 10), tuberculosis (3, 7, 11), atrial myxomas (7), mediastinal trauma (3, 5), thrombosis or phlebitis of the superior vena cava (5), and aortocaval fistula (3).

Treatment of the superior vena cava syndrome depends on the definite diagnosis established. In bronchogenic carcinoma involvement of the superior vena cava strongly suggests incurability and constitutes an ominous sign in almost every instance. Therapy in these patients often results in significant palliative improvement. Radiotherapy, together with nitrogen mustard treatment, are generally acceptable (1, 7) and patients may then be reevaluated for surgery.

As proposed by Urschel and Paulson (7), the use of a diuretic (chlorothiazide) in the acute stage offers prompt and consistent relief. Benign conditions are best left alone. Eventually collateral circulation will develop and the signs and symptoms will improve without the need for surgery, although occasionally surgical intervention is entertained by some surgeons.

In our particular case, the combination of radiotherapy and chemotherapy resulted in worthwhile palliation.

Summary

A case of superior vena cava syndrome due to malignant thymoma is reported. It is emphasized that early detection of the obstruction is difficult, definite diagnosis is most important, diuretics are useful in the acute stage and that venous collaterals usually will relieve the

obstruction in benign conditions.

Resumen

Hemos informado un caso de obstrucción de la vena cava superior producida por un timoma maligno. La detección temprana de la obstrucción es difícil, pero posible. Se enfatiza la importancia del diagnóstico definitivo, la ayuda de los diuréticos en la fase aguda y el rol de la circulación colateral para aliviar la obstrucción en las condiciones benignas sin necesidad de intervención quirúrgica.

Acknowledgments

Radiotherapy was administered at the Cancer League Hospital under the direction of Dr. Enrique Pantojas and chemotherapy at the San Juan City Hospital by Dr. Rafael Rizek. Pathologic examinations were performed by the Department of Pathology, Centro Médico de P. R., directed by Dr. Raúl Marcial Rojas.

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EDITORIAL

THE TRUE TASK OF THE PHYSIATRIST

We physiatrists have been criticized from oversimplifying our specialty, so that our therapists can take over our work, to overcomplicating our programs, so that the rehabilitation center goes bankrupt paying the high salaries of the different members of the "team". I do not intend to minimize the importance of the individual allied health professions that staff our rehabilitation centers, but I must limit my discussion today to the true task of the physiatrist. My only apology is to have selected such an extensive subject to discuss in such a short time.

First, let me point out that there is no field in medicine or surgery that will not benefit from consultation with physical medicine and rehabilitation. Accordingly, the physiatrist must be well-versed in the whole science of medicine. He must be able to recognize the cause and complication of disease as well as use his modalities of therapy. The physiatrist is a physician not a therapist. It is precisely his lack of knowledge of the former and his emphasis on the latter that has placed him in competition with his subordinates, the therapists. Thus, if the physiatrist practices as a therapist and not as a physician, he cannot blame his colleagues when they bypass him and send their patients directly to the therapist.

Let me illustrate with a simple problem, a peripheral paralysis of the facial nerve. Most physicians will diagnose this as a Bell's Palsy, prescribe Vitamin B12 injections and refer the patient for electrical stimulation. You and I both know that Vitamin B12 and electrical stimulation are not of very much value in curing this disease, but this treatment is the accepted one which most of us follow. In my practice, at least 10 percent of these patients are diabetics, and their peripheral palsy is not idiopathic but a manifestation of a diabetic neuropathy. In fact, I have at least 15 patients, the majority middle-aged, whose diabetes was discovered in my office because they presented primarily with a peripheral facial palsy. A physical therapist only stimulates the facial muscles; a physiatrist diagnoses diabetes mellitus as the cause of the paralysis.

As a physician, then, you must not only diagnose disease, but, also, you must be able to offer a prognosis. Most patients are more interested in the time of recovery than in diagnosis or treatment. Again, let me illustrate with a simple case. A beautiful young girl was preparing for her wedding when she was stricken with a Bell's palsy. She was heartbroken when she came into my office on the third day after onset and already had made plans to cancel her marriage. By performing a conduction time study on the facial nerve, which was 4.2 meters per second, I was able to assure her that she could proceed with her wedding, as she would recover completely in from 4 to 6 weeks. She was married in 4 weeks, and there was no sign of a peripheral facial palsy when she kissed the groom, and, of course, her doctor.

A physiatrist should write about his work in medical journals. Also, he should appear on medical panels, present papers at medical meetings, lecture not only to students at the university but to lay groups in church and club meetings, talk over radio and appear on TV programs sponsored by medical societies. In this day and age of competition, a new specialty, such as ours, is likely to be swallowed up by our own medical colleagues, who argue that we are invading their territories, and from the members of the rehabilitation team whom we, ourselves, have created.

This is also an era of specialization in the medical sciences. No longer is there one physician who

treats all systems, nor is there one surgeon who cuts on all the anatomy. We must emphasize that the physiatrist not only treats the whole man medically, but he goes even further and occupies himself with the social and economic aspects of his patient. As such, he is truly the only specialist today who presents the age-old image of the good physician so cherished by the patients and their families. We must let our colleagues and the public know, but in a strictly ethical fashion, about our work so they will acknowledge and respect our specialty.

Permit me to present this example. Several years ago, shortly after I published a paper on the value of the electromyogram in the diagnosis of the level of herniated lumbar nucleus pulposum, a school master was referred to me with a diagnosis of "Flail right lower extremity secondary to herniated lumbar disc" Upon examination of the patient, I found a flaccid paralysis of the right quadriceps with absence of the knee reflex and sensory loss confined to the anterior thigh surface. The clinical findings were characteristic of an anterior femoral neuropathy, rather than a L3-L4 root-compression syndrome. This was verified by electromyographic studies, because only the quadriceps muscle showed abnormal potentials. But more important, there was no summation, pointing to a complete paralysis of this muscle group. Although the patient was scheduled for a myelogram, I prevailed upon his physician to rule out the most likely causes of a peripheral neuritis first. Even though the patient had none of the characteristic symptoms of diabetes mellitus, his fasting blood sugar was 600 mgs. percent. Under specific treatment for diabetes, the paralysis began to disappear in six weeks. The patient was able to return to his work in a relatively short time and without the planned surgery.

Even in this modern era of medical specialization, the physiatrist, if need be, can lay claim to a body system as his own. As the cardiologist asserts his right to the heart, the dermatologist the skin, the neurologist the nerves and the orthopedist the bones, the physiatrist can demand the muscular system for himself with impunity. Today, the physiatrist is the expert in diseases of the muscle. If this is true, then he must know more about the anatomy, histology, physiology, pathology and treatment of muscular disorders than his colleagues.

Personally, I do not believe that we will ever gain the respect of our peers by being captains of rehabilitation teams. They will only respect us when they realize that we are more knowledgeable in diagnosing and treating all problems of the muscular system better than any other specialist. This is what I emphasize to my residents, and I plan their studies in the basic sciences primarily to encompass the muscular system.

However, they must also understand the function of the other body systems, perhaps as thoroughly as the other specialists. Since muscles connect to bone, they must study bone pathology and physiology. Since muscle action may be changed by orthopedic operations, they must understand these surgical procedures. Since muscle action is controlled by the central and peripheral nervous systems, they must study neuroanatomy, neurophysiology and neuropathology in addition to becoming well versed in neurology. They must know the heart in order to direct cardiac rehabilitation and be familiar with pulmonary function tests if they prescribe breathing exercises. This is acute medicine, and the physiatrist definitely must be knowledgeable in all these fields.

Now, it has been said that the physiatrist should deal only with the chronic or long-term diseased patients. This certainly is not the whole story. However, it is true that the specialty of physical medicine and rehabilitation came into being after World II with the care of the war-wounded paraplegics. Subsequently, what was learned in the rehabilitation of the severely wounded was transferred to the chronic arthritic, the hemiplegic and the psychiatric patient. The rehabilitation team composed of all the allied health professions under the direction of the physiatrist was found to be the most practical treatment regime. In fact it became so successful that, today, all the specialties have adopted this psychology of patient care.

Finally, a physiatrist works with specific tools common to his specialty. It is perhaps through our understanding and use of these diagnostic methods that we differ from our colleagues. First, we evaluate the muscles to determine their strength by means of a manual muscle test. Second, we measure the joints using a goniometer to test their range of motion. Third, we perform an evaluation of the activities of daily living, a check list of some 100-150 body functions, to determine the self-care possibility of our patients. Fourthly, we make use of specific electrodiagnostic studies to determine the activity of nerves and muscles. In addition, we work closely with our medical colleagues and the allied health professions to return all medical, surgical and psychiatric patients, in so far as possible, back into the mainstream of life as useful and taxpaying citizens.

Herman J. Flax, MD, FACP

SALE OR DISPOSITION OF A MEDICAL PRACTICE

(Prepared by The Office of the General Counsel of the American Medical Association)

INSURANCE

The physician will have several types of insurance policies in connection with his practice. Certainly, a conference with the insurance broker is indicated at an early date, but in general the following points can be noted. Any insurance to protect the physical assets against loss or accidental destruction, such as fire and theft insurance, can be cancelled once the ownership of the insured property is transferred to the purchaser. This is because one of the conditions of the policy is that the insured be the owner of the property. There will be a refund for the unexpired term of the policy. Likewise, any liability insurance policies on the doctor's premises may be cancelled after the premises are vacated, or after the purchaser takes over the office. This type of insurance protects the owner or occupier of the premises from liability to others who may be injured on the premises. There will be a return premium for the unexpired portion of the policy term.

Professional liability insurance, which is commonly referred to as "malpractice" insurance may be cancelled upon the physician's death, but the retiring physician should consider keeping his professional liability insurance in force if he expects to treat an occasional patient or to be at all available for consultation. Malpractice claims frequently do not arise for several years after the treatment is rendered, but it is the policy that was in effect at the time the treatment was rendered that will protect the physician or his estate, not the policy in effect when the claim is finally made. It is important, therefore, to retain the old policies, and to be able to identify the policies that were in effect in years past.

The physician probably also has some form of Workmen's Compensation insurance to protect him against liability to employees who may be injured while working. This insurance should not be cancelled while the physician, or his estate, still has employees working. When the actively practicing physician passes away suddenly, the physician's office staff can relieve much of the family's burden if they are asked to continue working until the practice is sold or until all necessary details connected with closing the practice have been completed. The continuing protection of the Workmen's Compensation insurance is necessary to provide for the possibility of injury to one of these employees.

Incidentally, in connection with the continued employment of the physician's office staff, do not overlook the fact that the employer is responsible for withholding income and social security (F. I. C. A.) taxes from the employee's earnings and

remitting same to the Government. Penalties and interest may attach for failure to file the necessary return and pay the tax due.

OFFICE MANAGEMENT

To a great extent, the method by which the physician operates his office will materially contribute to the ease or difficulty of disposing of his practice. If the physician has consulted with his lawyer on the broad spectrum of business organization problems, and if he has had an accountant set up his books of account and then has a bookkeeper make the appropriate entries in a reasonably prompt and regular manner, his office will operate efficiently, it will contribute to the confidence his patients place in him, and it will be very impressive to another physician who may be interested in purchasing the practice. The size and volume of the office will dictate the number of employees to efficiently operate the office. These employees, with proper training by the accountant or bookkeeper, can be charged with the duty of keeping the accounts payable and accounts receivable up-to-date, all correspondence current, and the complete field of taxes and insurance under control, so that the physician will not be in default in the payment of any taxes and will not suffer the danger of an insurance policy lapse. If the physician is fortunate enough to have employees who are most responsible, and in whom he has the highest degree of confidence, a great deal of the burden of office management can be lifted from his shoulders. However, he should never abdicate this responsibility entirely.

When the physician elects to retire and decides to sell his practice, he will find that his investment in proper office management will be a great help to him in making the sale. Furthermore, the family of the physician who has passed away will find comfort in knowing that the assets of the practice can immediately be marshalled and accurately evaluated. The up-to-date records will produce an accurate profile of the nature and condition of the practice. If the bookkeeper or the office manager can draw checks on a bank account designated for operating funds, current bills and taxes can be paid promptly, employees salaries can be continued while the office is maintained, fees collected and patients serviced with proper notification, cancelling or transferring appointments and properly transferring the medical records of patients where requested. These responsibilities would otherwise fall upon the family of the deceased physician, adding cruelty to their bereavement.

(To be continued)

NOTICIAS

CURRENT PROCEDURAL TERMINOLOGY, 3RD EDITION (CPT-3)

CPT-3 has been under revision for sometime and represents a considerable amount of effort on the part of many physicians.

Current Procedural Terminology (CPT-3) contains many new and useful additions. It has more than 2,000 new and revised procedures and services listed, making it the most comprehensive book of its kind. Also, a 74 page index has been included to provide easy access to any item; the Introduction and Guidelines have been expanded to simplify reporting.

It is believed that physicians will find CPT-3 a most valuable way of identifying and reporting their services. We will appreciate any effort on your part to inform your society members of the availability of CPT-3. Copies are obtainable from the Order Department of AMA at \$5.00 per copy.

US DOCTORS TO ATTEND YUGOSLAV ENVIRONMENTAL MEETING

Environmental health experts from throughout the world will attend an International Conference on Environmental Health next fall in Yugoslavia, the American Medical Association, one of the cooperating groups, announced.

The conference will be held Oct. 23-26, 1973, in Primosten, a resort area near the city of Split on the Adriatic Coast, the AMA reported.

Sponsored by the Union of Medical Societies of Yugoslavia with cooperation of the American Medical Association and the World Medical Association, the conference will be supported by the Bureau of Community Environmental Management, Health Services and Mental Health Administration, U. S. Department of Health, Education and Welfare.

The program is planned to stimulate an exchange of health and medical information with emphasis on specific programs and activities, epidemiological and other research, and consideration of prevention strategies, the AMA said.

A charter flight will leave Chicago Oct. 20 and arrive in Split the following day, with stopover in New York City for East Coast delegates. The return flight will leave from Geneva, Switzerland, Nov. 6 for Chicago, with stopover in New York. Those taking the charter flight will have an opportunity to plan individual vacations (Oct. 27-Nov. 5) following the conference. Several group or packaged tours will be offered for this period. Cost of the charter flight, round trip, will be approximately \$275.

Physicians, allied health professionals and others in the United States interested in attending the conference may obtain further details by writing to the Transportation Section,

American Medical Association, 535 N. Dearborn St., Chicago, Ill. 60610.

FIFTH INTERNATIONAL SEMINAR & EXHIBITION

This event will take place in THE CENTRAL HALL WESTMINSTER, LONDON, S. W. 1, from the 1st July - 5th July, 1974. The theme will be REHABILITATION OF DISABLED PEOPLE - THE NEW ERA.

Particulars: Conference Secretary, REHAB, Tavistock House (South), Tavistock Square, LONDON, WC1H 9LB.

FROM AMA HEADQUARTERS:

The Fourteenth National Conference on Physicians, Schools and Communities will be held in Chicago at the LaSalle Hotel October 4-5, 1973. The theme of this year's meeting is "Improving the Quality of Life: The Impact of Schools."

A special pre-conference meeting for physician representatives of medical societies will be held on the afternoon and evening of October 3, 1973 at the LaSalle Hotel. The meeting will provide a forum for medical societies to exchange ideas and activities related to the health of school aged children and youth. A portion of these special sessions will be devoted to a discussion of the Health Education Department's package program for medical societies and an examination of the services which the Department can provide.

We are unable to pay expenses for representatives. However, medical society representatives are invited to dinner on October 3rd.

We look forward to receiving the names of your representatives and will be glad to write directly to your nominees.

We will be very happy to answer any questions.

(Sgd.) Wallace Ann Wesley, Hs.D., Director

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(To be continued)

FE DE ERRATA

En el Boletín de enero 1973, Vol. 65, Núm. 1, fue publicado el artículo "Cerebrovascular and Peripheral Vascular Disease: Prevalence in Puerto Rican Males" — por los doctores Raúl Costas, Jr., Mario R. García Palmieri, Marcelino Cortés Alicea, Mercedes Cruz Vidal, Dolores Patterne y Angel M. Ayala.

Por un error involuntario, al hacer el Contenido, se cambió el nombre de la doctora Mercedes Cruz Vidal, co-autora, por el de la doctora Mercedes Vega Vidal.

Hacemos mención de este error en esta Fe de Errata.

Instrucciones para los Autores

El Boletín acepta para su publicación artículos relativos a medicina y cirugía y las ciencias afines. Igualmente acepta artículos especiales y correspondencia que pudiera ser de interés general para la profesión médica.

El artículo, si se aceptara, será con la condición de que se publicará únicamente en esta revista.

Para facilitar la labor de revisión de la Junta Editora y la del impresor, se requiere de los autores que sigan las siguientes instrucciones:

Manuscrito: El manuscrito completo, incluyendo las leyendas y referencias deberán estar escritos a máquina a doble espacio y por un solo lado de cada página, en duplicado y con amplio margen. En página separada deberá incluirse lo siguiente: título, nombre del autor (es) y su grado (ej: MD, FACP), ciudad donde se hizo el trabajo, el hospital o institución académica, patrocinadores del estudio, y si un artículo ha sido leído en alguna reunión o congreso, así debe hacerse constar como una nota al calce.

El manuscrito debe comenzar con una breve introducción en la cual se especifique el propósito del mismo. Las secciones principales (como por ejemplo: materiales y métodos) deben identificarse como un encabezamiento al centro y en letras mayúsculas.

Artículos referentes a resultados de estudios clínicos o investigaciones de laboratorio deben organizarse bajo los siguientes encabezamientos: Introducción, Materiales y Métodos, Resultados, Discusión, Resumen (en español e inglés), Reconocimiento y Referencias.

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Nomenclatura: Deben usarse los nombres genéricos de los medicamentos. Podrán usarse también los nombres comerciales, entre paréntesis, si así se desea. Se usará con preferencia el sistema métrico de pesos y medidas.

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Más de tres autores añadir: et al.

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In order to facilitate review of the article by the Editorial Board and the work of the printer, the authors must conform with the following instructions:

Manuscripts: The entire manuscript, including legends and references should be typewritten double spaced in duplicate with ample margins. A separate title page should include the following: title, authors and their degrees (e. g. MD, FACP), city where the work was done, hospital or academic institutions,

acknowledgment of financial sponsors, and if the paper has been presented at a meeting the place and date should be given.

The manuscript should start with a brief introductory paragraph or paragraphs which should state its purpose. The main sections (for example, Materials and Methods) should be identified by center headings in capital letters.

Articles reporting the results of clinical studies or laboratory investigation should be organized under the following headings: Introduction, Material and Methods, Results if indicated, Discussion, Summary in English and Spanish, Acknowledgments if any, and References.

Nomenclature: Generic names of drugs should be used; trade names may also be given in parenthesis, if desired. Metric units of measurements should be used preferentially.

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INDICE DE ANUNCIANTES

1. *Burroughs Wellcome - Empirin Compound \bar{c} Codeine*
2. *Ciba - Vioform HC*
3. *Geigy - Butazolidin alka*
4. *Roche - Dalmane, Efudex, Librium, Valium*
5. *Rorer - Maalox*
6. *Searle & Co. - Pro-Banthine*
7. *Upjohn - Unicap Therapeutic*

FUTUROS TRABAJOS A PUBLICARSE

1. **The Spectrum of Trifascicular Block** — Pablo Iván Altieri, MD, et al
2. **Tetanus in Southern Puerto Rico After a Mass Vaccination Program** — Alberto J. Larrieu, MD, et al
3. **Ausencia Congénita de los Músculos Abdominales - "Prune Belly"** - Reporte de un Caso — Luis C. Nina Ortega, MD
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5. **Influence of Alcohol on Traffic Deaths in Puerto Rico 1972** — Sidney Kaye, MD
6. **Efecto Nefrotóxico de los Agentes Antimicrobianos** — Rafael E. Ramírez González, MD

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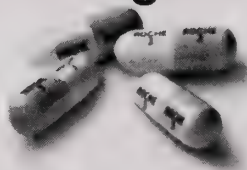
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Contraindications: Patients with known hypersensitivity to the drug.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation, or in women of childbearing age requires that its potential benefits be weighed against its possible hazards.

Precautions: In the elderly and debilitated and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruption, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increase and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

Supplied: Librium® Capsules containing 5 mg, 10 mg or 25 mg chlordiazepoxide HCl. Libritabs® Tablets containing 5 mg, 10 mg or 25 mg chlordiazepoxide.

BOLETIN

ASOCIACION MEDICA DE PUERTO RICO

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Junio 1973
Vol. 65, No. 6



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Everybody experiences psychic tension.



Most people can handle this tension.



Some people develop excessive psychic tension and need your counseling,



and a few may need counseling
and the psychotropic action of Valium® (diazepam).

Before deciding to make Valium (diazepam) part of your treatment plan, check on whether or not the patient is presently taking drugs and, if so, what his response has been. Along with the medical and social history, this information can help you determine initial dosage, the possibility of side effects and the ultimate prospects of success or failure.

While Valium can be a most helpful adjunct to your counseling, it should be prescribed only as long as excessive psychic tension persists and should be discontinued when you decide it has accomplished its therapeutic task. In general, when dosage guidelines are followed, Valium is well tolerated (see Dosage). For convenience it is available in 2-mg, 5-mg and 10-mg tablets.

Drowsiness, fatigue and ataxia have been the most commonly reported side effects.

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Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

Dosage: Individualize for maximum beneficial effect.

Adults: Tension, anxiety and psychoneurotic states, 2 to 10 mg b.i.d. to q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed; adjunctively in skeletal muscle spasm, 2 to 10 mg t.i.d. or q.i.d.; adjunctively in convulsive disorders, 2 to 10 mg b.i.d. to q.i.d. **Geriatric or debilitated patients:** 2 to 2½ mg, 1 or 2 times daily initially, increasing as needed and tolerated. (See Precautions.) **Children:** 1 to 2½ mg t.i.d. or q.i.d. initially, increasing as needed and tolerated (not for use under 6 months).

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Valium® (diazepam)

To help you manage excessive psychic tension

BOLETIN

ASOCIACION MEDICA DE PUERTO RICO



Organo Oficial

Fundado en 1903

Volumen 65

Junio 1973

Número 6

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CUBIERTA DEL MES DE JUNIO: IGLESIA SAN JOSE, VIEJO SAN JUAN
(Cortesía del XI Congreso Panamericano de Gastroenterología)



acute arthritic inflammation...heat that freezes

In acute rheumatoid arthritis consider Tandearil. The anti-inflammatory action of Tandearil quickly helps reduce heat, pain, swelling, and stiffness. Results are usually seen in 3 or 4 days. Try it for a week when the symptoms defy aspirin control.

Remember that Tandearil is not a simple analgesic. It should not be used on patients responding to routine therapy. Before using, please read the prescribing information. It's summarized below.

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Tablets of 100 mg.

Important Note: This drug is not a simple analgesic. Do not administer casually. Carefully evaluate patients before starting treatment and keep them under close supervision. Obtain a detailed history, and complete physical and laboratory examination (complete hemogram, urinalysis, etc.) before prescribing and at frequent intervals thereafter. Carefully select patients, avoiding those responsive to routine measures, contraindicated patients or those who cannot be observed frequently. Warn patients not to exceed recommended dosage. Short-term relief of severe symptoms with the smallest possible dosage is the goal of therapy. Dosage should be taken with meals or a full glass of milk. Patients should discontinue the drug and report immediately any sign of: fever, sore throat, oral lesions (symptoms of blood dyscrasia); dyspepsia, epigastric pain, symptoms of anemia, black or tarry stools or other evidence of intestinal ulceration or hemorrhage, skin reactions, significant weight gain or edema. A one-week trial period is adequate. Discontinue in the absence of a favorable response. Restrict treatment periods to one week in patients over sixty.

Indications: Acute gouty arthritis, rheumatoid arthritis, rheumatoid spondylitis.

Contraindications: Children 14 years or less; senile patients; history or symptoms of G.I. inflammation or ulceration including severe, recurrent or persistent dyspepsia; history or presence of drug allergy; blood dyscrasias; renal, hepatic or cardiac dysfunction; hypertension; thyroid disease; systemic edema; stomatitis and salivary gland enlargement due to the drug; polymyalgia rheumatica and temporal arteritis; patients receiving other potent chemotherapeutic agents, or long-term anti-coagulant therapy.

Warnings: Age, weight, dosage, duration of therapy, existence of concomitant diseases, and concurrent potent chemotherapy affect incidence of toxic reactions. Carefully instruct and observe the individual patient, especially the aging (forty years and over) who have increased susceptibility to the toxicity of the drug. Use lowest effective dosage. Weigh initially unpredictable benefits against po-

tential risk of severe, even fatal, reactions. The disease condition itself is unaltered by the drug. Use with caution in first trimester of pregnancy and in nursing mothers. Drug may appear in cord blood and breast milk. Serious, even fatal, blood dyscrasias, including aplastic anemia, may occur suddenly despite regular hemograms, and may become manifest days or weeks after cessation of drug. Any significant change in total white count, relative decrease in granulocytes, appearance of immature forms, or fall in hematocrit should signal immediate cessation of therapy and complete hematologic investigation. Unexplained bleeding involving CNS, adrenals, and G.I. tract has occurred. The drug may potentiate action of insulin, sulfonyleurea, and sulfonamide-type agents. Carefully observe patients taking these agents. Nontoxic and toxic goiters and myxedema have been reported (the drug reduces iodine uptake by the thyroid). Blurred vision can be a significant toxic symptom worthy of a complete ophthalmological examination. Swelling of ankles or face in patients under sixty may be prevented by reducing dosage. If edema occurs in patients over sixty, discontinue drug.

Precautions: The following should be accomplished at regular intervals: Careful detailed history for disease being treated and detection of earliest signs of adverse reactions; complete physical examination including check of patient's weight; complete weekly (especially for the aging) or an every two week blood check; pertinent laboratory studies. Caution patients about participating in activity requiring alertness and coordination, as driving a car, etc. Cases of leukemia have been reported in patients with a history of short- and long-term therapy. The majority of these patients were over forty. Remember that arthritic-type pains can be the presenting symptom of leukemia.

Adverse Reactions: This is a potent drug; its misuse can lead to serious results. Review detailed information before beginning therapy. Ulcerative esophagitis, acute and reactivated gastric and duodenal ulcer with perforation and hemorrhage, ulceration and perforation of large bowel, occult G.I. bleeding with anemia,

gastritis, epigastric pain, hematemesis, dyspepsia, nausea, vomiting and diarrhea, abdominal distention, agranulocytosis, aplastic anemia, hemolytic anemia, anemia due to blood loss including occult G.I. bleeding, thrombocytopenia, pancytopenia, leukemia, leukopenia, bone marrow depression, sodium and chloride retention, water retention and edema, plasma dilution, respiratory alkalosis, metabolic acidosis, fatal and nonfatal hepatitis (cholestasis may or may not be prominent), petechiae, purpura without thrombocytopenia, toxic pruritus, erythema nodosum, erythema multiforme, Stevens-Johnson syndrome, Lyell's syndrome (toxic necrotizing epidermolysis), exfoliative dermatitis, serum sickness, hypersensitivity angitis (polyarteritis), anaphylactic shock, urticaria, arthralgia, fever, rashes (all allergic reactions require prompt and permanent withdrawal of the drug), proteinuria, hematuria, oliguria, anuria, renal failure with azotemia, glomerulonephritis, acute tubular necrosis, nephrotic syndrome, bilateral renal cortical necrosis, renal stones, ureteral obstruction with uric acid crystals due to uricosuric action of drug, impaired renal function, cardiac decompensation, hypertension, pericarditis, diffuse interstitial myocarditis with muscle necrosis, perivascular granulomata, aggravation of temporal arteritis in patients with polymyalgia rheumatica, optic neuritis, blurred vision, retinal hemorrhage, toxic amblyopia, retinal detachment, hearing loss, hyperglycemia, thyroid hyperplasia, toxic goiter, association of hyperthyroidism and hypothyroidism (causal relationship not established), agitation, confusional states, lethargy; CNS reactions associated with overdosage, including convulsions, euphoria, psychosis, depression, headaches, hallucinations, giddiness, vertigo, coma, hyperventilation, insomnia; ulcerative stomatitis, salivary gland enlargement. (B)98-146-800-F (10/71)

For complete details, including dosage, please see full prescribing information.

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Opinion & Dialogue

"Prescription drugs – who should determine the maker?"

Dispenser of Medicine

Clifton J. Latiolais
President
American
Pharmaceutical
Association



Maker of Medicine

C. Joseph Stetler
President
Pharmaceutical
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"Too many doctors are indifferent to the economic consequences of their decisions." So stated a recent issue of *Medical News Report* (December 4, 1972), an independent weekly newsletter published by former AMA Chief Executive F. J. L. Blasingame, M.D.

Doctor, are you indifferent...?

In discussing an anticipated increase in Blue Shield rates, Dr. Blasingame's newsletter had this to say:

"In general, it can be said, MD's have given the impression they are not particularly concerned with the increase in cost of health care to their patients...

"True, an MD's training is primarily scientific, but in the real world of practice, all of his scientific decisions have a price tag, or an economic impact. The economics of health care beckon the practitioner's attention. Concern for economics of medicine

When the pharmacist recommends that a drug product other than the one ordered be dispensed, the prescriber invariably permits the change when he feels the best interests of the patient will be served.

Shortcomings of Pro-Substitution Argument

The fact remains that it is necessary for the prescriber to know that the change is being contemplated, and to be in a position to consent or demur. Without that opportunity, the unilateral decision of the pharmacist, made in the absence of clinical knowledge of the patient, could expose him to needless risks, and in addition, jeopardize the relationship between the professions of Pharmacy and Medicine. In my view, there is nothing in the pro-substitution argument that offsets these risks.

The Issue of Drug Knowledge

Substitution advocates claim that the primary justification for changing the rules is the desire to better utilize pharmacists' knowledge about drugs. Yet the pharmacist's task to keep current on the entire field of drug therapy, to some degree, puts him at a disadvantage. Most often, a practicing physician will need expert knowledge of no more than 25

should be an obligation of medical practice...

"Medical societies ought to conduct continuing campaigns to point out the substantial savings that could be realized thru deductible insurance and protection for catastrophic illnesses. At the very least, they should, in the patients' interest, question the tactics of any insurance organization that raises health care costs by forcing policyholders to buy insurance they may not need or want and probably won't ever use.

"Too many doctors are indifferent to the economic consequences of their decisions. Too many, for example, habitually hospitalize patients for the convenience of the MD. It's nonsense to deny such habits exist...

"Doctors, thru their medical societies, have unhesitatingly appealed to their patients for support in the fight against government interference with the private practice of medicine. And the public in the past has responded. It's time the American Medical Association and state and local medical societies paid off the debt by decisive action to hold down the cost of medical care."

Cost of Drugs

Insurance rates and hospital charges are only two factors in health

care costs. The cost of drugs—both prescription and nonprescription—is another.

And when it comes to drug costs, the nation's pharmacists are *concerned*. Through their national professional society, the American Pharmaceutical Association, pharmacists are advising the public to use nonprescription medication cautiously and conservatively, and to seek the advice of their pharmacist before selecting or purchasing such drugs.

Outdated Laws

The pharmacist also is aware that when it comes to prescription drugs, often he has an even greater opportunity to reduce the cost to the patient—with no sacrifice in the quality of the medication dispensed. But in many states, outdated and antiquated laws prevent the pharmacist from engaging in drug product selection. "Drug product selection" simply means that the pharmacist functions in the patient's interest by consciously choosing, from the multiple brands available, a low-cost quality brand of the specific drug to be dispensed in response to the physician's prescription order.

Much *misinformation* has been purposely spread by those who stand to gain financially by maintaining

high drug costs to the public. An endless stream of propaganda has emanated from the drug industry in an effort to persuade the medical profession that these so-called anti-substitution laws should be retained. And as long as these laws are retained, the drug industry will continue its current marketing practices which contribute unnecessarily to high drug costs to patients. These practices also are inviting government agencies to expand their restrictive controls on physicians and pharmacists.

APhA Efforts

As pharmacists, we are concerned about health care costs. We hope that every physician shares our concern on this vital issue, and will give his personal support to the constructive efforts APhA has undertaken in the interest of all patients.

(For a complete discussion of drug product selection, you are invited to request a free copy of the "White Paper on the Pharmacist's Role in Product Selection" from: American Pharmaceutical Association, 2215 Constitution Avenue, N.W., Washington, D.C. 20037.)

of 30 drugs that he selects to treat the majority of conditions encountered in his practice. Moreover, the physician's choice of a specific brand is based on his knowledge of the patient's medical history and current condition, and his experiences with the particular manufacturer's product.

Some substitution proponents have argued that the dispensing of a prescription is a simple two-party transaction between the pharmacist and the patient, and that a substituting pharmacist may avoid even a technical breach of contract by simply notifying the patient that he is making the substitution. I would judge that the courts would be sympathetic toward a pharmacist who substituted without physician approval and who undertook a legal defense that seeks to make the patient responsible for the pharmacist's actions.

Reduced Prescription Prices?

Substitution advocates are suggesting to the consumer, and particularly the consumer activist, that reduced prescription prices could follow legalization of substitution. We have seen absolutely no evidence to justify this claim. To the contrary, experience in Alberta, Canada, where substitution is authorized, suggests

the opposite.

Many pharmacists understandably are concerned about the cost of maintaining multiple stocks of similar products. While there is no doubt that inventory costs rise when additional brands are stocked, it would be interesting to know how much they rise, and how many pharmacists actually stock *all* brands—of, say, ampicillin or tetracycline—or how long they keep "slow moving" products on their shelves before they are returned for credit. To ask that the industry eliminate multiple sources is to ask competitors to stop competing.

Drug Substitution—A License for the Unethical

Anti-substitution repeal would favor "corner cutting" pharmacists and manufacturers. For them, free substitution would be not a right, but a license. As an aftermath, it is quite likely that the confidence of both physicians and patients in the profession of Pharmacy would be eroded, as revelations about the unconscionable behavior of an undisciplined few were magnified in the press or in professional circles.

Summary

In short, what the American Pharmaceutical Association advo-

cates as a broad-spectrum panacea looks to us to be not only a minority view (advocacy of substitution is by no means a uniform policy in Pharmacy), but also an extraordinarily costly and ineffective remedy, whose side effects are odious. We believe (1) that an impressive majority of pharmacists prefer to work with Medicine and with industry, for the consumer, and for the general good, (2) that they seek the privilege to substitute when the patient might gain and when the patient's doctor agrees, and (3) that they seek to work for the resolution of genuine grievances openly and professionally.

(For amplification of PMA views, please write for our booklet, "The Medications Physicians Prescribe: Who Shall Determine the Source?" It is available from: Pharmaceutical Manufacturers Association, 1155 Fifteenth Street, N.W., Washington, D.C. 20005.)

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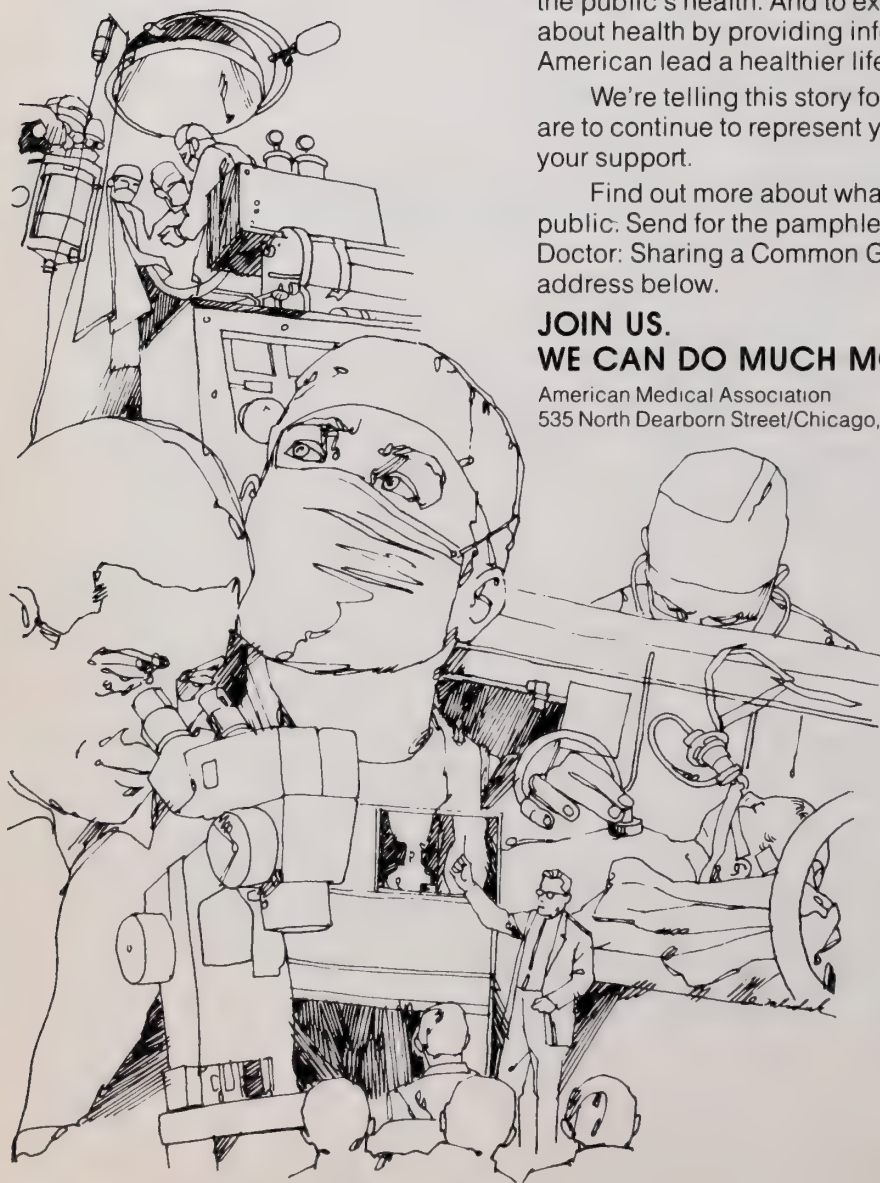
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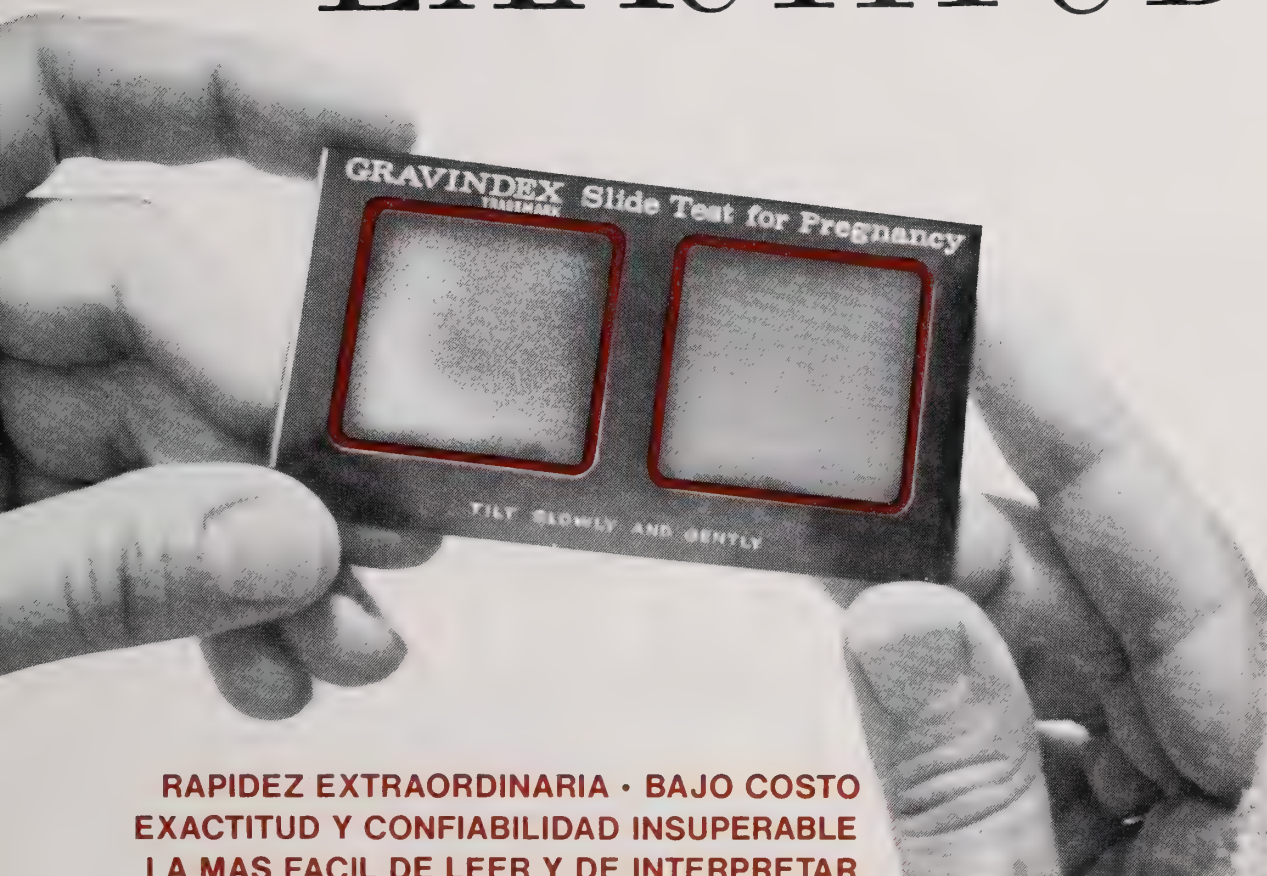
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GRAVINDEX

Marca de Fábrica

LA PRUEBA EN LAMINA DE 3 MINUTOS QUE DETECTA EL EMBARAZO



ORTHO DIAGNOSTICS

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**What's
on your
patient's
face...**

**may be more important than
his chief complaint**

The lesions on his face may be solar/actinic — so-called 'senile' keratoses...and they may be premalignant.

Solar, actinic or senile keratoses

These lesions may be called by several names, but they usually can be identified by the following characteristics: the typical lesion is flat or slightly elevated, of a brownish or reddish color, papular, dry, rough, adherent, and sharply defined. They commonly occur as multiple lesions, chiefly on the exposed portions of the skin.



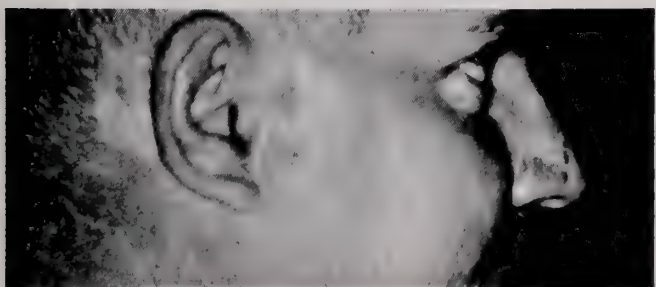
Patient P.T. seen on 3/29/67 shows typical lesions of moderately severe keratoses. Note residual scarring on ridge of nose from previous cryosurgical and electro-surgical procedures.*

Sequence of therapy/ selectivity of response

After several days of therapy with Efudex® (fluorouracil), erythema may begin to appear in the area of the lesions; the reaction usually reaches its height of unsightliness and discomfort within two weeks, declining after discontinuation of therapy. This reaction occurs in affected areas. Since the response is so predictable, lesions that do not respond should be biopsied.

Acceptable results

Treatment with Efudex provides highly favorable cosmetic results. Incidence of scarring is low. This is particularly important with multiple facial lesions. Efudex should be applied with care near the eyes, nose and mouth.



Patient P.T. seen on 6/12/67, seven weeks after discontinuation of 5%-FU cream. Reaction has subsided. Residual scarring not seen except for that due to prior surgery. Inflammation has cleared and face is clear of keratotic lesions.*

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Multiple actinic or solar keratoses.

Contraindications: Patients with known hypersensitivity to any of its components.

Warnings: If occlusive dressing used, may increase inflammatory reactions in adjacent normal skin. Avoid prolonged exposure to ultraviolet rays. Safe use in pregnancy not established.

Precautions: If applied with fingers, wash hands immediately. Apply with care near eyes, nose and mouth. Lesions failing to respond or recurring should be biopsied.

Adverse Reactions: Local — pain, pruritus, hyperpigmentation and burning at application site most frequent; also dermatitis, scarring, soreness and tenderness. Also reported — insomnia, stomatitis, suppuration, scaling, swelling, irritability, medicinal taste, photosensitivity, lacrimation, leukocytosis, thrombocytopenia, toxic granulation and eosinophilia.

Dosage and Administration: Apply sufficient quantity to cover lesion twice daily with non-metal applicator or suitable glove. Usual duration of therapy is 2 to 4 weeks.

How Supplied: Solution, 10-ml drop dispensers — containing 2% or 5% fluorouracil on a weight/weight basis, compounded with propylene glycol, tris(hydroxymethyl)aminomethane, hydroxypropyl cellulose, parabens (methyl and propyl) and disodium edetate.

Cream, 25-Gm tubes — containing 5% fluorouracil in a vanishing cream base consisting of white petrolatum, stearyl alcohol, propylene glycol, polysorbate 60 and parabens (methyl and propyl).

**This patient's lesions
were resolved with**

**Efudex®
(fluorouracil)**

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*Data on file, Hoffmann-La Roche Inc., Nutley, N.J.

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TETANUS IN SOUTHERN PUERTO RICO AFTER A MASS VACCINATION PROGRAM

Alberto J. Larrieu, MD
Lucio García Moliner, MD
Héctor F. Rodríguez, MD

Mortality from tetanus was a major public health problem in Puerto Rico until 1965 with a morbidity 10 times that of continental United States (1, 2).

In 1965-66 the Department of Public Health initiated a mass vaccination program for the control of this disease. In all 68 percent of the population received at least one dose of vaccine. The school age group (5-15 yrs.) had the highest percentage of vaccinated subjects (83 percent), while those over 20 years of age had the lowest (51 percent) (2).

The present study was undertaken to determine the effects on incidence, mortality and general characteristics of tetanus, in the years following the previously mentioned mass immunization program.

Method and Results

All cases of tetanus hospitalized in the Department of Medicine and Pediatrics of the Ponce District Hospital from January 1, 1966 to June 30, 1972, were analyzed. There were 128 patients. The distribution by department and by year is shown in Fig. 1 with higher incidence in adults, 93 cases, compared to 35 children. The disease affected adult males more often (54 males-39 females), but in pediatric patients, the sex distribution was similar (18 males-17 females). Peak incidence occurred in 1966 with a total of 43 cases, with a constant decline since then (Fig. 1). Please note that in 1969 the Department of Medicine had 19 admissions for the disease, and there were none in the Pediatric Department.

The mortality observed is shown in Table I. There were 41 deaths for a mortality of 32 percent without significant difference between adults and children. In the adult group, the death rate was equal in both sexes. A higher mortality (39 percent) was found in male children as compared to females (23 percent) although the difference is not statistically significant.

From the Department of Medicine Ponce District Hospital and the University of Puerto Rico School of Medicine.

Presented at the Annual Meeting of the Medical Society of the Southern District on December 8, 1972 at Ponce, P. R.

Request for reprints should be addressed to: A. J. Larrieu, MD, Dept. of Surgery, Univ. of Maryland Hospital, Baltimore, Md.

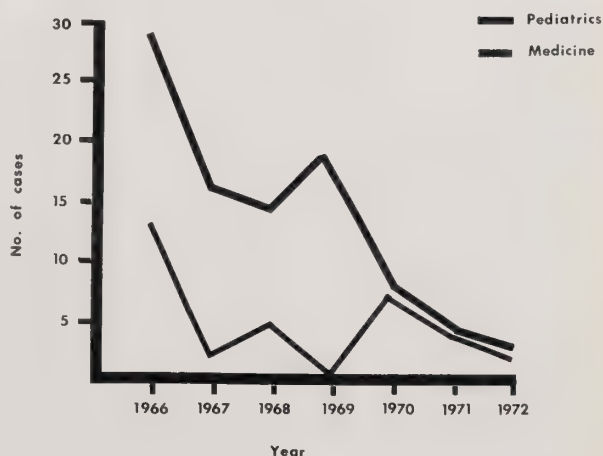


Fig. 1: Tetanus cases admitted by years and service.

TABLE I

	Admissions	Deaths
<i>Medicine:</i>		
Males	54	17
Females	39	13
Total -	93	30
<i>Pediatrics:</i>		
Males	18	7
Females	17	4
Total -	35	11
Overall Mortality in Series:	32.03 percent	
	128 cases — 41 deaths	

Case fatality rate by age is shown in Fig. 2. A high mortality occurred in the very young and in the elderly, with a 71 percent mortality rate for tetanus neonatorum and close to 60 percent in subjects over 70 years old. Although the median age of all patients, excluding neonates, was 38 years, the average at death was 55 years. There were two other variables which influenced prognosis adversely, besides the age factor: a short incubation period and the rapidity of progression of symptoms, especially if generalized convulsions appeared.

The interval between trauma to the onset of symptoms could be ascertained in 83 patients (Table II). Fifty had an incubation period of less than one week, of these, 22 died, for a mortality of 44 percent. In those with an incubation period over one week only 6 of 33 patients died, for a mortality of 18 percent.

Symptomatology was an important prognostic factor. It was found, as noted by Dr. Rodríguez et al (1), that the presence of convulsion within 48 hours after the appearance of symptoms was an ominous sign. As shown in Table III, 81 percent of these patients died. However, if convulsions developed after 48 hours, the mortality was 30 percent, whereas in patients in whom no convulsions occurred, only 13 percent died.

Since the presence of these three previously discussed factors increases the mortality to nearly 100 percent, these patients are in need of the most sophisticated and aggressive therapeutic methods available, such as controlled respiratory therapy, neuro muscular blocking agents under continuous supervision and hyperbaric oxygen therapy (3).

The overall mortality in this series was 32 percent, which is 4 percent higher than the one reported in the previous study, but still significantly lower than the death rate informed here and in the United States (2, 4, 5, 6).

Discussion

A significant and gradual decrease in the incidence of tetanus in Southern Puerto Rico, has occurred from 64 cases per year as reported in 1965, to 19 patients per year in our series (1966-1972) (1). An overall reduction has also been reported by others (2, 7). Notwithstanding, our morbidity is still 10 times higher than that of continental United States. It should also be emphasized that in 1969 and 1970 close to 70 percent of the cases of tetanus in Puerto Rico were reported in Ponce and the rest of the southern health region (7).

Evident in fig. 3, the greatest reduction in incidence occurred in children, and at present, children constituted 28 percent of the total series contrasting with the previous study (1), in which the pediatric cases accounted for 50 percent. Thus, the trend is that tetanus now affects adults perhaps due to greater lack of adequate tetanus immunization of adults in contrast to infants and children (2, 4).

The high mortality of tetanus neonatorum noted (Fig. 2) again emphasized how important immunization is, not only of women in their childbearing age but also of those pregnant during their routine pre-

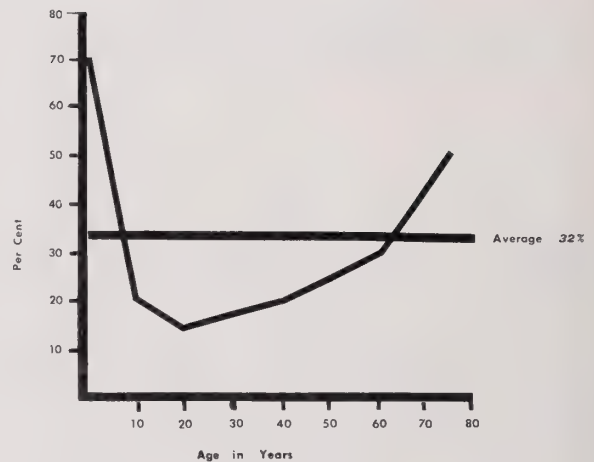


Fig. 2: Case fatality by age groups.

TABLE II

Incubation Period	No. of Patients	Deaths	Mortality
Less than 1 week	50	22	44 percent
Over 1 week	33	6	18 percent

TABLE III

Convulsions in Tetanus			
Onset	Cases	Deaths	Percent
Within 48 hrs.	26	21	80.8
Over 48 hrs.	10	3	30
No convulsions	84	11	13

natal care as the best method to curtail the terribly high mortality of tetanus in neonates (2, 8, 9). The other peak in the fatality rate involves the elderly who may combine inadequate immunization with debilitating diseases. Noteworthy, this group was com-

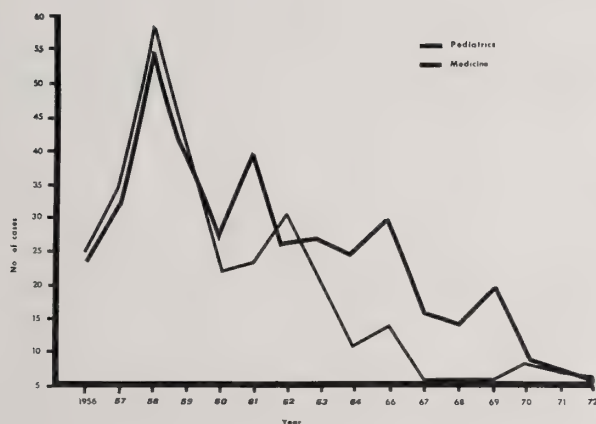


Fig. 3: Tetanus cases admitted by years and service.

posed by some patients without evidence of trauma, but with cronically infected leg ulcers, a probable portal of entry for the tetanus bacillus. Presented with this type of patient, adequate care of these leg ulcers as well as immunization of these individuals, is mandatory.

We believe in spite of our island-wide immunization programs, that tetanus still remains a major public health problem in Puerto Rico, especially in two groups: neonates and adults over 40. Intensive programs should be continued with routine immunization of pregnant women to eliminate tetanus neonatorum and concerted efforts carried out to reach adults over 40. We can again state: "As active immunization with tetanus toxoid will most certainly prevent the disease, there is no excuse for anyone to develop tetanus or die from it".

Therapy had four main objectives:

1. Neutralization of the neurotoxin before it combined irreversibly with the central nervous system.
2. Proper sedation and control of convulsions.
3. Debridement, cleansing, and elimination of the focus of infection.
4. Management of complications and establishment of supportive therapy.

Up to 1966, tetanus antitoxin was utilized in doses of 100,000 U. to neutralize the neurotoxin. Since 1967, however, the use of tetanus immune human globulin has been utilized as much as its relatively high price allows us. The agent has several advantages over the heterologous sera: it does not need sensitivity testing; it has a half life ten times longer than that of

serum from other species; and a protective effect with one tenth of the dosage of tetanus antitoxin (8, 10). The dose used by us is 5,000 U. of the human immune globulin. Phenobarbital and Promazine (Sparine) are still our preferred drugs for sedation and control of convulsions. Diazepam (Valium) has also been used in some cases, especially in Pediatrics (8, 11). Penicillin remains the antibiotic of choice to eradicate the focus of infection in doses of 600,000 U. daily. In patients with penicillin allergy, erythromycin is utilized. Local cleansing and debridement retains its importance especially in the presence of chronic ulcers.

General supportive management of these patients is important, especially in patients with severe trismus, opisthotonus or those requiring tracheostomy. Parenteral hyperalimentation is being considered as an added supportive measure in the near future (12).

Although the group of patients undergoing tracheostomy showed a high mortality this procedure is usually carried out in patients with extremely poor prognosis such as patients with early convulsive seizures, and in the elderly. Corticosteroids are not used routinely but rather in selected cases showing severe toxicity and high fever. Last, but not least, is skilled nursing care. Hampered at times by shortage of personnel, the role of our paramedical personnel is most important. Our nurses have become extremely proficient in the care of these tetanus patients.

Summary

A study of 128 cases of tetanus from the Department of Medicine and Pediatrics of the Ponce District Hospital, encompassing the period from January 1, 1966 to June 30, 1972, is presented. The incidence of tetanus, especially in children, has decreased after the mass vaccination program undertaken in 1965-66. In spite of this, our morbidity is still ten times higher than the United States. It is interesting to note that in 1969 close to 70 percent of the cases of tetanus reported in the island occurred in Southern Puerto Rico.

A mortality of 32 percent is found in this series and the factors that modify prognosis and the therapeutic regime are discussed. Finally, it is concluded, that although much has been attained by the island-wide immunization program, tetanus still remains a major public health problem in Puerto Rico, especially in two groups: Neonates and Adults over 40.

Resumen

Se presentan los resultados de un estudio de 128

casos de tétano de los Departamentos de Medicina y Pediatría del Hospital de Distrito de Ponce, ingresados entre enero 1, 1966 a junio 30, 1972.

Ocurrió una disminución significativa en la incidencia de tétano, especialmente en niños, desde que comenzó el programa de vacunación en masa en 1965-1966. Sin embargo, nuestra morbilidad es todavía diez veces la de los Estados Unidos. Se señala también que durante los años 1969-70 cerca del 70 por ciento de los casos de tétano informados en la isla ocurría en la parte sur de Puerto Rico, especialmente en dos grupos: Neonatos y Adultos sobre 40.

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INFLUENCE OF ALCOHOL ON TRAFFIC DEATHS IN PUERTO RICO — 1972

Sidney Kaye, PhD

Alcohol: The Number One Drug Problem

The homicides (traffic deaths) on our highways in Puerto Rico not only continues — but it continues to get worse each year. Traffic deaths are again on the increase in Puerto Rico. This is so shameful and such a horrible way to die. Although many factors are involved in the cause and manner of these traffic deaths, one thing is certain; alcohol plays a major role as an influencing factor (1, 2, 3). It was found in 1968 (4), 1969 (5), 1970 (6), and again in 1971 and 1972 that more than 50 percent of the total traffic fatalities were influenced by alcohol. If only we could stop this “senseless, irresponsible traffic drinking”, we might then cut these traffic deaths in half. This however, will not be easy because alcoholism is by far, the *number one* drug problem in Puerto Rico. It has been estimated that there are about 1 million “potential drinkers” out of a total population of 2.8 million people in Puerto Rico (7); the ‘true’ figures are not known.

It was formerly thought that it was the social drinker (who is by far in the majority) who caused and produced most of these fatal accidents (1). This was found not to be true in the United States (2), nor was it true in Puerto Rico in 1969 (5), 1970 (6), and again in 1971 and 1972. It is the heavy (problem) drinker who (although in the minority) is causing and producing most of these traffic fatalities. We must in some way identify this problem drinker, and try to rehabilitate him. Alcoholism is a disease of man, which is only exceeded in number by heart disease, mental disease and cancer. The problem drinker (alcoholic) is one who drinks to such an extent and in such a manner as to

injure his health, his ability to make a living and thus economically and socially affects his family. In other terms (medically): an alcoholic is also one who has compulsion, tolerance, and withdrawal symptoms. His “sickness” affects many persons (directly and indirectly) including doubling the number of senseless killings on our highways.

Statistical Data

In 1972 with a population of about 2,830,000 persons; 793,884 registered vehicles; 650,187 drivers, there are 3,695 miles of highway; and on these highways there were 77,765 traffic accidents that resulted in approximately 26,500 personal injuries and 552 deaths (8, 9).

Of the total 552 traffic deaths, we were able to study in some measure 404 that were submitted for blood alcohol levels and for drug studies following an autopsy. Of these, 296 were autopsied at the Institute of Legal Medicine (School of Medicine) of the University of Puerto Rico. 108 specimens were sent from the rest of the Island; thirty eight from the Arecibo District Hospital, thirty six from the Fajardo District Hospital; twelve from the Ponce District Hospital; and twenty two from Mayagüez and Aguadilla District Hospitals.

During 1972, there were 552 traffic deaths on our highways in Puerto Rico. It is an all time record for Puerto Rico; this represents a sharp increase of 15.5 percent over the last year (478).

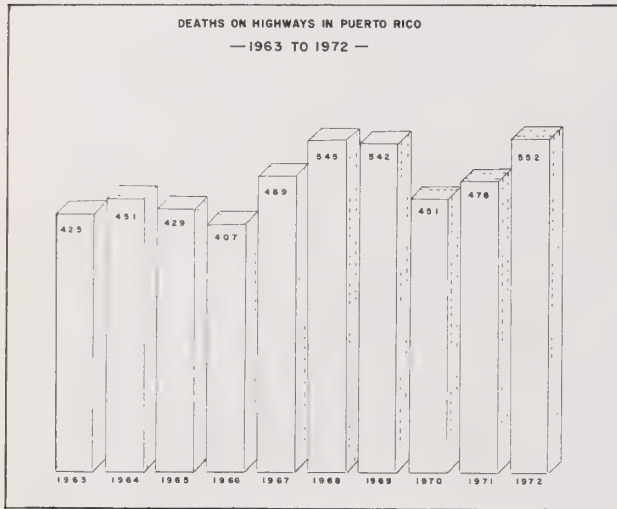
Of the total 552, we have studied 404, of which 296 were autopsied at the Institute of Legal Medicine (School of Medicine) University of Puerto Rico.

The 404 traffic fatalities that were studied, were separated and categorized as to pedestrian, driver, passenger, age, sex, occupation, day of week, hour of day. Only those persons over 15 years old and who died within 5 hours of the accident were analyzed for (presence and amount of) alcohol in blood and common depressant drugs and carbon monoxide.

With this data assembled, it was again shown that males outnumber females 5:1 (334M - 83 percent and 70F - 17 percent). This follows the same trend

From the Institute of Legal Medicine, School of Medicine, University of Puerto Rico.

This investigation was supported by the Puerto Rico Highway Safety Commission; Safety Project AL 52-73-18, and by a Grant from the U. S. Department of Transportation, Federal Highway Administration, Bureau of Highway Safety.



as in 1968 when it was 5:1; in 1969 it was 4:1, in 1970 it was 4:1, and in 1971 it was 4:1.

In Puerto Rico, the pedestrian continues as in previous years to account for the *majority* of our traffic deaths studied. This year the pedestrians accounted for 189 cases (150M - 79 percent and 39F - 21 percent); or 47 percent of the total 404 cases studied. This is in sharp contrast to the drivers who accounted for 23 percent (93) of the total traffic deaths studied. In this group there were 86 males and only 7 females. In ratio, males by far outnumber the female by about 12 to 1 in the "fatal driver" category.

The passengers accounted for 19 percent (76 cases; 55M:21F). The remaining 46 were: motorcyclist 9, bicyclist 3, horseman 1, tractor operators 3; in 30 cases the categories were not established.

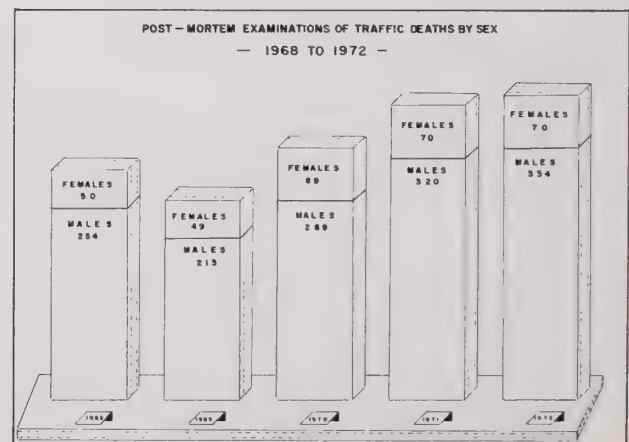
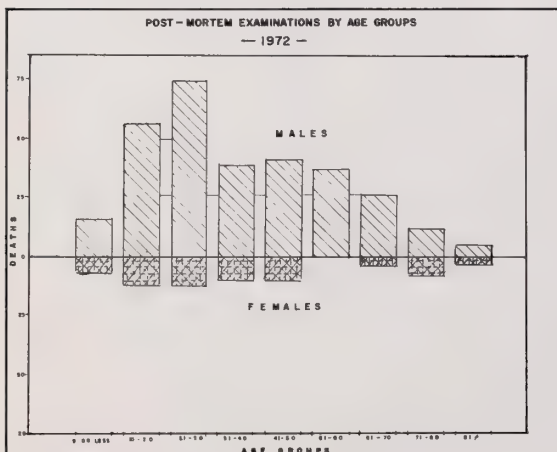
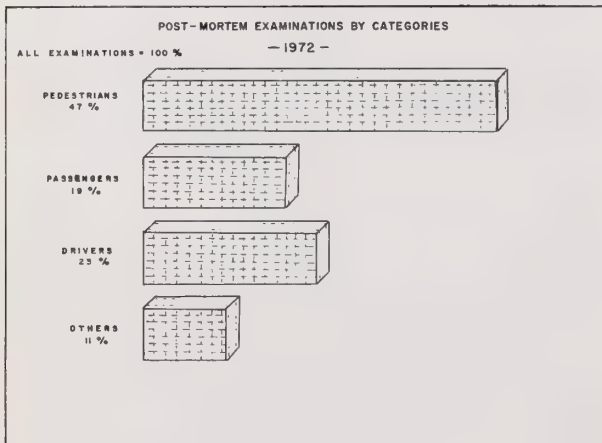
Pedestrian

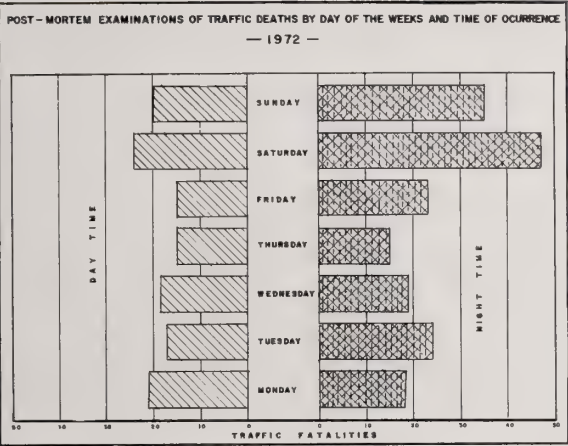
As in 1968, 1969, 1970, 1971 and again 1972, the pedestrian contributed by far to the majority of our traffic fatalities. All ages totalled 189 (150M:39F). The largest representative age group was between 51-60 yrs, with 33 deaths (all males).

The occupation of the pedestrians studied fell into these categories: First laborers, next housewives and next students.

Driver

Drivers accounted for 93 highway deaths or 23 percent of the total studied. There were only 7 females to 86 males (1:12). The age group that contributed the most fatalities was 21-30 yrs. with 47 deaths (33M: 3F). Males by far outnumber females. As to occupation of these drivers, laborers were first with businessmen next, and office clerks next.





Time and Day of Fatal Traffic Accident

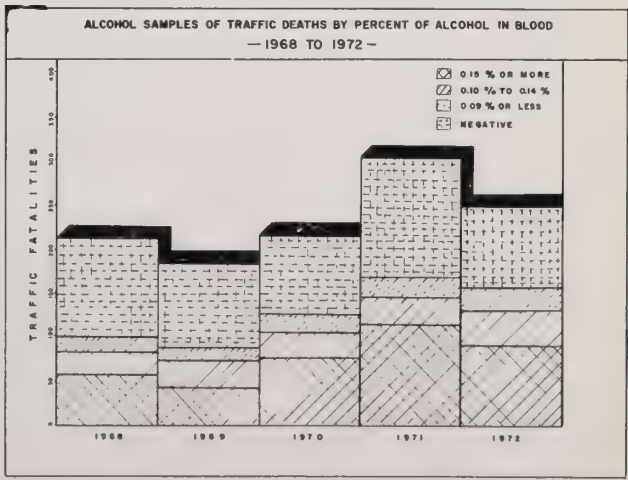
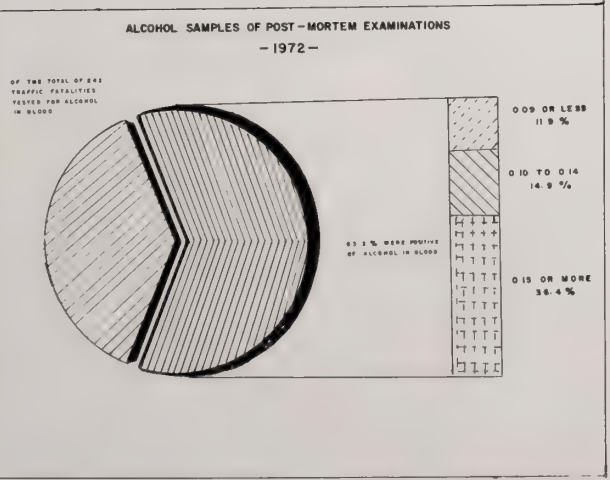
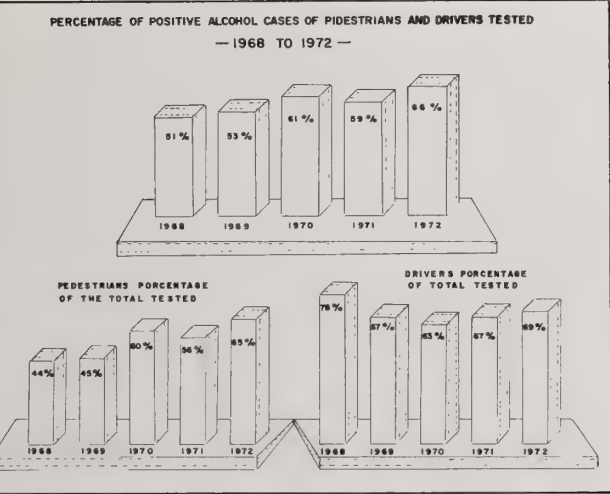
The distribution of the fatal cases by day of week and hour of occurrence, again shows that most deaths occurred during Sunday and Saturday with 149 (37 percent) cases out of the total of 404. Of these 149 cases, 126 were males and 23 were females. Tuesday follows with 54 cases (42 males and 12 females), then Monday with 47 cases Friday with 46 cases; Wednesday with 42 cases and finally Thursday with 34 cases. There were 32 cases where the day of the accident was not clearly established.

With the distribution by hour (time of day) of occurrence, it was noted that 181 (58 percent) out of 311 occurred during the night (that is from 6:00 pm to 5:59 am). Of these 181 "night time" cases, 134 (74 percent) occurred from 6:00 pm to 12:00 midnight. 130 traffic death accidents occurred during the day time and in 93 or (23 percent) cases, the hour of the accident was not clearly established.

Alcohol Levels in Blood

In 242 cases of the total of 404 post-mortem examinations, blood alcohol levels were determined. In the remaining 162 cases, no blood alcohol was determined because of the long interval of time elapsed between accident and the death and also no blood alcohol was determined on persons under 15 years old.

Of the total of 242 cases analyzed for blood alcohol content, 153 (63.2 percent) were positive, 144 males and 9 females, or a proportion of males over females of 16:1. The remaining 89 (36.8 percent) cases were alcohol negative in the blood sample of which 63 were males and 26 were females.



When we distributed the 153 positive cases of alcohol by categories, that is, in pedestrians, drivers, passengers, etc. We found that 68 cases were pedestrians, 63 males and 5 female. This is 44.4 percent of the total of 153 positive alcohol cases and 64.8 percent of all pedestrians tested (105). Next were the drivers with 45 positive alcohol cases (43 males and only two female). This is 29.4 percent of the total positive alcohol cases and 69.2 percent of the total drivers tested (65). The passengers follows with 21 positive alcohol cases of this (20 males and one female). This is 13.7 percent of the total positive alcohol cases and 48.8 percent of the total passengers tested. The motorcyclist contributed with 9 cases, 1 horseman, 3 tractor operators and for 30 cases the categories were not established.

The total positive cases were separated by day of the week. This separation demonstrated that Saturday accounted for the largest number of positive alcohol cases with 38 (25 percent), then followed by Sunday with 28 (18 percent) then Friday with 20 cases (13 percent). In other words, these three days accounted for 86 (56.2 percent) positive alcohol cases of the total of 153. The remaining 67 cases were distributed in the remaining days of the week, that is, Monday and Tuesday with 13 cases each and Wednesday and Thursday with 11 cases each. In 19 cases the day of the week was not established.

When we separated the positive alcohol traffic fatality cases by hours of occurrence, we noted that 87 out of 153 cases occurred during the night, and only 27 occurred during the day time. In 37 cases the hour of the accident was not clearly established. Of the total night fatal accidents, 64 (73.6 percent) of them occurred between 6:00 pm to 12:00 midnight.

A combination of the day of the week and hour of occurrence of all positive alcohol cases shows us that 87 (56.9) cases occurred during night time, 64 of them from 6:00 pm to 12:00 midnight. In other words 7 out of 10 victims die in accidents during the night. Friday, Saturday, and Sunday (weekend) accounted for 86 cases of which 52 of the victims died during the night. Most of these (35) died from 6:00 pm to 12:00 midnight.

In 88 of these fatal traffic cases, the level of alcohol in blood was established at 0.15 percent or more. This is 57.5 percent of the total positive cases. From 0.10 to 0.14 percent group there were only 36 cases or 23.5 percent; and in only 29 cases (19.0 percent), the alcohol level in blood was established at 0.09 percent or less.

Age group sex distribution that showed most positive alcohols.

32 males - Ages 21 to 30 had the largest number of positive alcohol.

6 females - Ages 31 to 50 had the largest number of positive alcohol.

Sex distribution of driver and pedestrian positive for alcohol.

Driver - 43 males and 2 females

Pedestrian - 63 males and 5 females

Percent comparison of previous years of driver and pedestrian positive for alcohol.

Year	Pedestrian	Driver
1968	44 percent	78 percent
1969	45	67
1970	60	63
1971	56	67
1972	65	70

Incidence of Depressant Drugs

Any depressant drugs or gases can be expected to effect the driving ability of an individual. A survey was initiated in Puerto Rico in 1968 to analyze for the presence of these depressant drugs and for carbon monoxide gas in traffic fatalities. They were found occasionally present.

In 1972 there were 9 positive cases found:

1 morphine derivatives (F)

4 Phenothiazines derivatives (3M:1F)

4 barbiturate derivatives (3M:1F)

Of these 9 positive depressant drug cases, 4 were also positive for alcohol.

We found a total of 27 cases positive (1-40 percent, 1-20 percent, 3-15 percent, 9-10 percent, 13-5 percent) for carbon monoxide. Nineteen of these were also positive for alcohol.

Summary

Alcohol abuse is definitely the number one Drug Problem in Puerto Rico and in the United States of America. In 1972 traffic deaths continued to rise and continued to be the largest cause of death due to accident. There were 552 traffic deaths per 2.8 million population and more than 50 percent of these again were influenced by the presence of alcohol (as in 1968, 1969, 1970 and 1971).

Even more sad is the fact that 58 percent of the

total positive alcohol related traffic deaths in Puerto Rico showed 0.15 percent alcohol or above. This is not social drinking but represents very *heavy drinking*.

It is very interesting to note that in Puerto Rico the pedestrian deaths continue to outnumber driver deaths 2 to 1, and that we had very few alcohol positive females that were killed on our highways. In 1970 not one single female "alcohol positive" driver was killed on our highways; in 1971 only one; in 1972 it is now 2. Will this continue to increase?

The alcohol related fatal traffic deaths were found to be concentrated on the evenings of Sunday, Friday and Saturday in this sequence.

In addition to the problem of the "drinking pedestrian and driver", we now again have evidence of depressant drug and carbon monoxide related traffic fatalities.

In 1972 we found 9 positive drug cases:

1 morphine derivatives (1F)

4 Phenothiazine derivatives (3M:1F)

4 Barbiturate derivatives (3M:1F)

It is interesting and gratifying to note that there is a decrease from 4 positive morphine traffic-deaths in 1971 (3M:1F), now to 1 (F) in 1972. Is this significant?

Carbon monoxide (car exhausts) was found positive in 27 cases, 19 of which were also positive for alcohol.

How can we stop this slaughter on our highways? If only we could identify the problem drinker and keep him off our highways, we would then cut this death toll tremendously. Of less problem (but still a definite threat) is the presence of carbon monoxide and depressant drugs. The drug users (legitimate or otherwise) must be cautioned as to its dangers while driving. Carbon monoxide can be produced by faulty car exhaust system and/or smoking.

Acknowledgments

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NOTE: A complete list of tables will be furnished upon request with reprint.

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THE SPECTRUM OF TRIFASCICULAR BLOCK

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The human intraventricular conducting system operates as a trifascicular system (1, 2). The depolarization of the ventricles occurs through the right bundle branch (RBB), the anterior and posterior divisions of the left bundle branch (LBB) (Fig. 1). Each of the divisions have different morphologic characteristics and are related to different structures; even their blood supply is different. Because of these reasons the two more vulnerable segments are the RBB and the anterior division of the LBB. These are followed in decreasing order of vulnerability by the main LBB, the main bundle and the posterior division of the LBB (1).

If there is a block of the anterior division of the LBB the electrophysiologic pattern of the left anterior hemiblock (LAH) will be produced. Block in the posterior division of the LBB will produce a left posterior hemiblock (LPH). Table I and II shows the criteria for the diagnosis of pure LAH and LPH. Eleven varieties of distal fascicular intraventricular block have been described, included in this group are the trifascicular blocks or block in the RBB and in the two divisions of the LBB (Table III) (1).

These divisions are affected by several processes including coronary disease, myocarditis, Lev's disease, Lenegre's disease, cardiomyopathies, ostium primum defects (1-2), rheumatic carditis (3) and recently as a familial autosomal dominant heritable disorder (4).

It is the purpose of this paper to discuss the spectrum of trifascicular blocks.

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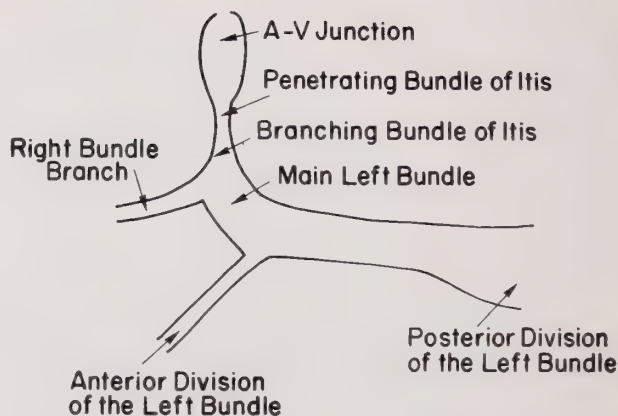


Fig. 1: Drawing showing the five main fascicles of the intraventricular conduction system. These are the bundle of His (with the penetrating and branching portions), the left bundle branch with its anterior and posterior divisions and the right bundle branch.

TABLE I: CRITERIA FOR THE DIAGNOSIS OF PURE LEFT ANTERIOR HEMIBLOCK (LAH)

1. Mean axis between -45° and -60° .
2. Q waves in leads I and AVL.
3. Q1 S3 pattern.
4. QRS is narrow, never wider than 0.10 seconds.
5. Voltage of R1, S2 and S3 are moderate.

Myocarditis Causing Trifascicular Block

Involvement of the conduction system in acute myocarditis of various causes leading to atrioventricular block is infrequent. In 1950 Lilienfeld reported a case

TABLE II: CRITERIA FOR THE DIAGNOSIS OF PURE LEFT POSTERIOR HEMIBLOCK (LPH)

1. Mean axis around $+120^\circ$, provided the forces of the first half of the QRS complex are also directed toward $+120^\circ$.
2. $S_1 Q_3$ pattern.
3. Tall R waves in leads II and III provided a vertical heart or right ventricular hypertrophy can be excluded.
4. Left ventricular disease is proven.

TABLE III: INTRAVENTRICULAR BLOCKS

1. Block in the anterior division of the LBB (LAH).
2. Block in the posterior division of the LBB (LPH).
3. Block in both divisions of the LBB (complete LBBB).
4. Block in the main LBB.
5. Right bundle branch block (RBBB).
6. RBBB with LPH.
7. RBB with LAH.
8. LBBB with LAH *.
9. LBBB with LPH *.
10. Block in the two main bundle branches (Bilateral Bundle Branch Block).
11. Trifascicular Block

* LBBB has to be partial.

of myocarditis due to sulfonamide sensitivity. The patient had a typical right bundle branch block (RBBB) with left anterior hemiblock (LAH) and an axis in the frontal plane of -75° . Two days later another electrocardiogram showed the RBBB, but with a change in axis to $+165^\circ$ (posterior hemiblock) (LPH). In subsequent electrocardiograms the RBBB disappeared and the axis changed to $+60^\circ$. This is an example of intermittent RBBB, LAH and LPH (5).

Harris et al reported a case of chronic idiopathic myocarditis and intermittent complete atrioventricular block. Her electrocardiogram showed LPH, CRBBB with 2:1 A-V block and eventually complete heart block due to permanent trifascicular bundle branch block. The pathologic examination revealed organizing myocarditis with fibrosis of the summit of the ventricular septum associated with severe old destruction of the left bundle branch, more recent partial destruction of the right bundle branch, and acute degeneration and inflammatory changes mostly of the branching portion of the A-V bundle, the bifurcation and both bundle branches. They

brought the point of the possible salutatory effect of corticoids in the treatment of acute A-V block, and this patient showed a definitive temporary improvement after their use (6).

Rosenbaum has reported several cases of trifascicular block due to chronic chagasic myocarditis. During an epidemiologic survey in a highly endemic area in Argentina, LAH was found to be present in 45 cases (23.7 percent) out of 189 subjects of all ages (in 25 cases, together with RBBB) in which serologic tests for chagasic disease were positive.

We reported a case of rheumatic carditis causing acute trifascicular block (3). He had aortic and mitral involvement and his clinical and electrographic changes improved markedly with steroids.

An electrocardiogram done on admission showed a regular rhythm with an axis in the frontal plane of -70° (LAH), P-R interval of 0.21 seconds and incomplete right bundle branch block (ICRBBB). The P waves were inverted in V6, suggesting "left atrial rhythm". These findings were compatible with the diagnosis of trifascicular block; although when either RBBB with LAH or LPH are accompanied by a prolonged P-R interval, the latter block may occur in the other division of the left bundle branch (LBB), in the main LBB, in the common bundle or in the A-V node. The recording of His bundle potentials may help to rule out the A-V node and main bundle as the site of the A-V block, but recordings from the main LBB itself would be needed to determine whether additional block occurs at the level of the main LBB or of the other division. However, the existence of RBBB with LAH in patients with marked left ventricular dysfunction strongly suggests that the additional affected fascicle is located at the ventricular level.

As we see any inflammatory process of the myocardium can involve the conduction system and cause hemiblocks or trifascicular blocks. As has been shown steroid therapy may be beneficial in some cases, especially during acute inflammatory processes.

Coronary Disease causing Trifascicular Block

Alterations of the three fascicles of the conduction system by a number of different disease entities, including coronary disease, cause eight different possibilities of intraventricular and atrioventricular conduction disturbances classified as trifascicular blocks and hemiblocks (1-2). These are: 1) RBBB with intermittent LAH and LPH, 2) RBBB, LAH and LPH, all permanent (trifascicular, complete heart block), 3) permanent

RBBB and LPH with intermittent LAH, 4) permanent RBBB and LAH with intermittent LPH, 5) permanent LPH with intermittent RBBB and LAH, 6) permanent LAH with intermittent RBBB and LPH, 7) RBBB, LAH and LPH all intermittent and 8) permanent LPH and LAH with intermittent RBBB.

The case of an 83 year old female patient with coronary disease who had an electrocardiogram done on May 9, 1969 (Fig. 2a) at 4:00 p.m. and it showed an axis in the frontal plane of -60° (LAH), CRBBB and a P-R interval of .12 sec. The ST segments were depressed from V1-V6. Two hours later, the electrocardiogram (Fig. 2b) showed an axis of -60° (LAH, CRBBB, a P-R interval of .12 sec and giant T waves in V4-V5. An electrocardiogram done at 7:00 p.m. (Fig. 2c) showed an axis of $+120^{\circ}$ (LPH), a P-R interval of .16 sec and prominent peaked T waves in V2-V5. The electrocardiogram done on May 13 (Fig. 2d) showed an axis of -60° (LAH), CRBBB and the P-R interval was .21 seconds, probably due to delay conduction in the posterior division of the left bundle.

The previous case was an example of acute trifascicular block after ischemic myocardial injury due to atherosclerotic heart disease, but also there are cases of chronic trifascicular block, frequently, explained by lesions in the small coronary branches although this cannot be included in the entity called coronary atherosclerosis. As a result there is vascular insufficiency, possibly induced by mechanical stresses applied to smaller coronary vessels in the area of the cardiac conduction system. The studies of Sabiston and Gregg (7) have shown that intramyocardial tension impairs the blood supply of the heart and Kirk and Honig (8) have demonstrated that subendocardial perfusion is deficient relative to the rest of the myocardium. They attributed this phenomenon to a higher tissue pressure in the endocardial surface of the left ventricle. Subendocardial damage has been shown in patients with left ventricular hypertrophy (9-10) and in myocardial necrosis due to norepinephrine infusion (11). Perhaps in some old patients there is insufficient blood supply to the subendocardium (where the conduction system is located) causing anoxic damage to the system and as a result of this, conduction problems.

Several authors have reported that right bundle branch block with abnormal left axis deviation proceeds the development of symptomatic A-V block. They attributed the abnormal left axis deviation to a block in the anterior division of the left bundle.

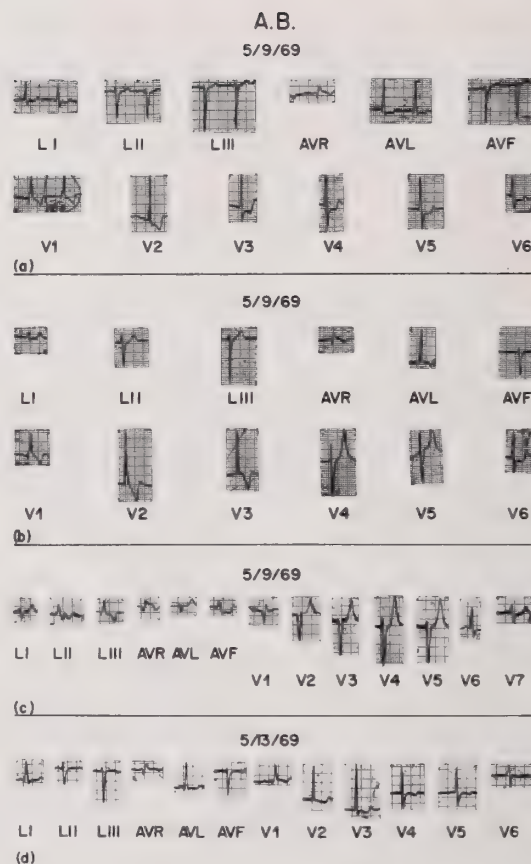


Fig. 2: Electrocardiograms showing an acute trifascicular block. See text for description.

This pattern has been interpreted as a form of bilateral bundle branch block but less emphasis has been placed on the fact that CRBBB with right axis deviation can also be a precursor of symptomatic A-V conduction disturbances (2, 13, 15, 17). Usually this combination occurs when there is extensive myocardial damage because the posterior division of the left bundle is the best protected part of the conductive system (2). Of course, it is well recognized that CRBBB with right axis deviation frequently occurs in patients with right ventricular hypertrophy, pulmonary disease, extremely vertical hearts or massive lateral wall infarctions.

Castellano reported in 1970 five cases of acute trifascicular block and he pointed out the high incidence of A-V block and mortality in these patients because CRBBB plus LPH presupposes significant septal and bundle branch lesions due to a massive anterior wall infarction (14). Several authors have reported a

high mortality in patients with acute trifascicular block, because of the frequent complications, mainly cardiogenic shock, complete heart block with Adam-Stokes episodes and asystole. That is why we think temporary intravenous pacemakers should be inserted, in all patients with acute trifascicular block due to ischemic heart disease.

It is important to remember that "false negative" diagnosis of myocardial infarct could be done in the presence of hemiblocks. For example, LAH by substituting an initial R wave in inferior leads in some cases can eliminate the expected Q waves of diaphragmatic infarct (2). In anteroseptal myocardial infarction the Q waves expected in the right precordial leads may, with the onset of LAH, be replaced by R-waves and in this way the anteroseptal myocardial infarct may be masked (2). Figure 3 shows the unusual case of a LAH concealing an old inferior and anteroseptal myocardial infarct. In LAH the initial 10m sec vector is directed inferiorly due to unopposed conduction over the left inferoposterior fascicle of the left bundle branch. If the depolarized inferior walls is not involved by the infarct then these forces may conceal the inferior myocardial infarct. These inferior forces are usually not recorded in the chest leads. However, if the chest leads are registered slightly below the conventional level in LAH a small R wave may be recorded. This may obliterate the Q waves of an anteroseptal myocardial infarction, as seen in Fig. 3. This can produce small Q waves in the right chest leads if the latter are recorded above the electrical center of depolarization (emphysema or of high application of the chest electrodes). Simulation of anteroseptal infarct can also occur in pure LPH, misleading Q waves may appear in the right precordial leads if the electrodes are applied below the conventional level.

Another example of "false positive" is when LAH leads to the development of impressive, Q waves in lead AVL and thus simulates high lateral wall infarct. That is why in the presence of hemiblocks the recording of the precordial leads, should be done below and above the conventional place. Sometimes the electrocardiogram should be complemented by the vectorcardiogram.

Post Surgical Trifascicular Blocks

The occurrence of complete heart block or right bundle branch block after surgical repair of tetralogy of Fallot and ventricular septal defect is well known (18, 19). These complications are related to the

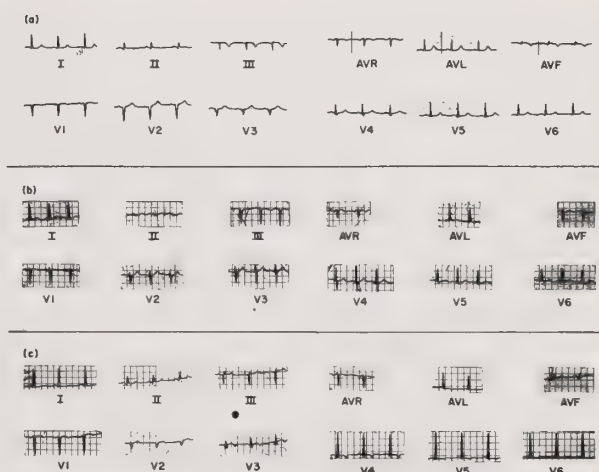


Fig. 3: LAH concealing an old inferior and anteroseptal myocardial infarct. See text for description.

proximity of the conduction system to the postero-inferior border of ventricular septal defects of the infracristal type, involving the membranous septum (20, 21). The proximal segment of the anterior division of the left bundle branch is also closely related to the inferior border of the membranous septum and it shares similar anatomic relations with the first portion of the right bundle branch (2). LAH could be seen after this type of surgery.

Rosenbaum reported four cases in which LAH with RBBB developed after surgery (22). The post-operative tracings were similar to the electrocardiograms of RBBB with LAH seen in acquired heart disease. Rarely do you see LPH after surgery because the fibers forming the posterior division of the left bundle are given off early from the main bundle. By doing that, they depart from the vicinity of the defect; the fibers of the anterior division leave the bundle more distally and, therefore, are more closely related to the inferior border of the defect and to the initial segment of the right bundle.

LAH occurred in approximately 5 percent of their cases of surgically repaired tetralogy of Fallot (22). On the other hand, the incidence of right bundle branch block has been shown to be much higher (23, 24).

Recent work by Gelband suggest that the RBBB seen after surgery is not due to closure of the ventricular septal defect, but is related to the right ventriculotomy. If this is the case there is normal conduction through the right bundle and the block is more peripherally (25).

This group of patients with RBBB with LAH should be followed closely, because they are prone to develop

ventricular arrhythmias, sudden death and complete heart block (26).

According to Lev, supported by Hudson, the bundle of his can be composed of two segments; penetrating and branching. The penetrating portion of the bundle travels from the distal end of the A-V node to the point where the initial radiation of the left bundle branch are given off, after it emerges from the central fibrous body at the level of the noncoronary aortic cusp (2).

The branching portion extends from the point where the bundle starts to emit the most posterior fibers of the left bundle, to the point which marks the origin of the right bundle and the most anterior fibers of the left bundle. Its proximal end, which is the continuation of the penetrating segment, lies at the level of the posterior third of the noncoronary aortic cusp; its distal end, which is a most strategic area in the entire ventricular conduction system, lies at the level of the line separating the noncoronary from the right coronary aortic cusp. Then we could see that a lesion or surgery of the aortic valve, if it extends to the bundle, will mostly injure its distal branching segment, and will thus be commonly associated with block in some of the subdivisions, especially the right bundle branch and the anterior division of the left bundle (2).

The case of a 50 year old male patient (JL) who had aortic valve replacement because of a bicuspid valve with severe aortic stenosis. Electrocardiogram before surgery showed only left ventricular hypertrophy. After surgery he developed left axis deviation (LAH), CRBBB and a maximal P-R interval of .21 seconds (Fig. 4a). The patient has been doing well, keeping a heart rate of about 70-80 beats per minute. Probably manipulation in the area near the conduction system caused complete block in the anterior division of the left bundle and in the RBBB. The prolonged P-R interval could be due to delay conduction through the posterior division then the term trifascicular block would apply, delay conduction through A-V node, or even delay conduction throughout the atrium. The exact explanation of the prolonged P-R interval can be done only by bundle of His or left bundle recordings.

As we see, surgery near the conducting system of the heart may cause serious conduction problems due to trauma to the fascicles.

Trifascicular Blocks in Congenital Heart Disease

As discussed before the most common cause of

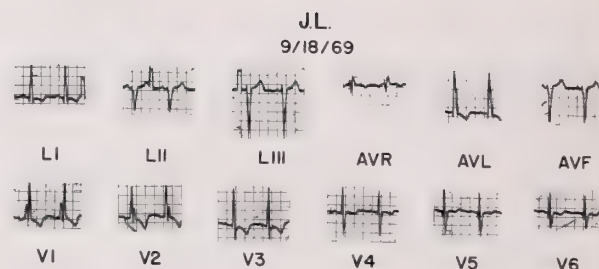


Fig. 4: Electrocardiogram showing a LAH with right intraventricular conduction defect, and a P-R interval of .21 sec. See text for description.

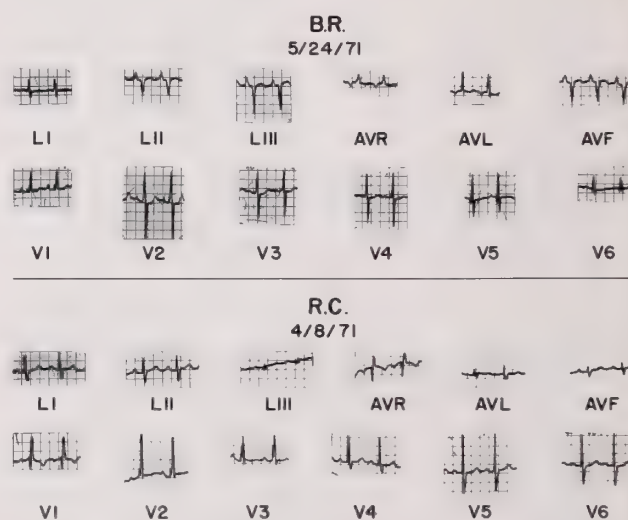


Fig. 5: Electrocardiograms of two patients with atrioventricular canal defects. See text for description.

RBBB with LAH in the adult are coronary heart disease, the cardiomyopathies, Lenegre's disease, Lev's disease and aortic valvular disease. The most common causes in children with congenital heart disease are the different varieties of common atrioventricular canal (2). The mechanism through which blocks are generated in these congenital cases included "mechanical" elongation and stretching of the conduction system and anomalous development of the anterior division of the left bundle, in some cases (2). Another explanation is that these electrocardiographic changes are due to faster conduction through the posterior division of the left bundle, but it is difficult to visualize occurrence of faster conduction as the result of a pathologic process (27).

In figure 5 the two electrocardiograms are from patients with different varieties of common atrioventricular canal.

The first electrocardiogram (BR) is of a female pa-

tient with ASD plus VSD and it shows left axis deviation (LAH), CRBBB and the longest P-R interval was .21 sec probably delay conduction through the posterior division of the left bundle.

The second electrocardiogram is that of a patient (RC) with Down Syndrome with the diagnosis of endocardial cushion defect. There is left axis deviation (LAH) CRBBB and the longest P-R interval was .21 sec probably delay conduction through the posterior division of the left bundle.

Idiopathic Causes of Trifascicular Blocks

Lenegre reported 62 cases in which histological study disclosed severe lesions in both bundle branches, and found in 11 only sclerodegenerative lesions of the conduction system, whereas the myocardium and the coronary arteries were spared (28, 29). Davies and Harris (30) described the lesions, "the initial change is vacuolization of the conduction fiber with fusion of myofibrils into a hyaline mass." Yates et al (31) regarded the lesion as anoxic, the exact nature of this process is unknown. According to Lenegre, these cases usually start with RBBB subsequently followed by LAH and finally complete heart block. Lenegre's disease should always be considered a forerunner of complete heart block and it should be suspected clinically in middle-aged or elderly people in whom high-grade A-V block and Adams-Stokes seizures developed abruptly. Usually the chest x-ray will be within normal limits and coronary angiography will show normal coronary arteries.

Under the name of "Sclerosis of the left side of the cardiac skeleton," Lev described a process that causes progressive fibrosis and calcification of the mitral annulus, the central fibrous body, the pars membranacea, the base of the aorta, and the summit of the muscular ventricular septum (32).

Rosenbaum has pointed out, that Lev's disease is responsible for most of the cases of RBBB with LAH seen in elderly persons. The patients usually show no other sign of cardiac involvement and only uncommonly do they develop complete heart block. He stressed that RBBB plus LAH, due to involvement of what he has called "pseudo bifurcation" of the bundle of His, seems to be the most common fingerprint of Lev's disease, and is usually related to sclerosis of the summit of the muscular septum. The prognosis is benign.

Are there two entities caused by anoxia to the conduction system due to the so called "small artery disease", to an unknown metabolic process causing

intracellular anoxia or are they caused by mechanical trauma to the conduction system? It is interesting that we studied a group of patients with "angina like chest pain with angiographically normal coronary arteries", and we found a high incidence of electro and vector cardiographic abnormalities, which suggested that the chest pain is cardiac in origin (33). Other investigators have shown anaerobic metabolism in a similar group of patients. Are these patients the ones who develop the hemiblocks and trifascicular blocks? It will be interesting to follow these patients to see their outcome.

Functional Trifascicular Blocks

Due to aberrancy in the conduction system the electrocardiographic patterns of LAH, LPH, RBBB and LBBB and any possible combination of patterns could be seen. These patterns are physiologic because they usually occur in a normal conduction system. In general they occur because (1) Recovery takes longer in the conduction system than in the myocardium or A-V junction, (2) Recovery varies from fascicle to fascicle.

Frequently these physiologic patterns are seen in patients having premature atrial beats or atrial fibrillation.

Summary

The human intraventricular conducting system operates as a trifascicular system. Due to several processes, eight different possibilities of blocks have been described. These are (1) RBBB with intermittent LAH and LPH (2) RBBB, LAH and LPH, all permanent (3) Permanent RBBB and LPH with intermittent LAH (4) Permanent RBBB and LAH with intermittent LPH (5) Permanent LPH with intermittent RBBB and LAH (6) Permanent LAH with intermittent RBBB and LPH (7) RBBB, LAH and LPH, all intermittent (8) Permanent LAH, LPH with intermittent RBBB.

The spectrum of the trifascicular blocks includes all eight possibilities caused by myocarditis, coronary disease, surgically induced, congenital (A-V canal defects), as a dominant heritable disorder and idiopathic (Lenegre's and Lev's disease).

Resumen

El sistema de conducción intraventricular opera

como un sistema trifascicular. Ocho diferentes posibilidades de alteraciones de conducción conocidas como bloqueos trifasciculares o hemibloqueos han sido descritas, éstas son: (1) Bloqueo de la rama derecha con bloqueo intermitente del fascículo anterior y posterior de la rama izquierda, (2) Bloqueo de la rama derecha y de los fascículos anterior y posterior, todos permanentes, (3) Bloqueo permanente de la rama derecha y del fascículo posterior con bloqueo intermitente del fascículo anterior, (4) Bloqueo permanente, de la rama derecha y, del fascículo anterior con bloqueo intermitente del fascículo posterior, (5) Bloqueo permanente del fascículo posterior, con bloqueo intermitente de la rama derecha y del fascículo anterior, (6) Bloqueo permanente del fascículo anterior con bloqueo intermitente de la rama derecha y del fascículo posterior, (7) Bloqueo intermitente de la rama derecha y de los fascículos anterior y posterior, (8) Bloqueo permanente de los fascículos anterior y posterior con bloqueo intermitente de la rama derecha.

El espectro de los bloqueos trifasciculares incluye las ocho posibilidades causadas por miocarditis, enfermedad obstructiva coronaria, quirúrgicamente ocasionados, heredados con una tendencia dominante, congénitos (canal atrioventricular) e idiopáticos (enfermedad de Lenegre y Lev).

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PROBLEMS CONCERNED WITH THE
DIAGNOSIS AND TREATMENT OF
OVARIAN CARCINOMA

Langdon Parsons, MD

Ovarian cancer is a separate entity and we are a little unhappy that the results of therapy have not measured up to our expectations. Ovarian cancer is not a single entity but a whole spectrum of diseases. Each component has its own origin, its own particular biological behaviour and a completely individualized growth pattern. We will first review what we do know about ovarian cancer in general.

1. Cancer of the ovary is on the increase. It is now the leading cause of death in New York State. The death rate from cancer of the ovary is roughly three times what it was forty years ago. More women are reaching the age where we commonly encounter it and we can expect to see more of it in the future.

2. Diagnostic aids have little value in the early diagnosis of ovarian cancer. This is unfortunate for the prognosis is definitely linked to the extent of the disease.

3. Growth pattern is insidious and that there are no pathognomic symptoms.

4. Tumor has spread beyond the ovary in four fifths of the cases when they are first seen.

5. It is simply impossible to differentiate a benign neoplasm from a malignant one on the basis of the history, even with your hand at the time of the abdominal exploration unless the tumor has spread beyond the ovary.

6. All the solid tumors, except the Thecoma and Fibroma have some degree of malignant potential. All metastases to the ovary are solid tumors, regardless of their point of origin.

7. We must surgically explore. The final diagnosis depends on the pathologist's interpretation of the tissue presented to him. This may be possible on frozen section specimens. The extent of the surgical attack may well be influenced by the histology. Since the growth pattern may vary in different parts of the same tumor, particularly in cystic papillary tumors, the pathologist should be given the entire tumor mass for a single biopsy may not be enough.

Every ovarian neoplasm should be considered malignant: (1) abdominal exploration is not only indicated, it is mandatory; (2) the basic treatment should be bila-

teral salpingo-oophorectomy combined with total hysterectomy when the neoplasm is malignant, regardless of the age of the patient. This may be radical therapy for the young woman who would like to preserve menstrual and reproductive function. If possible we would like to find a reasonably conservative approach.

When cancer is confined to the ovary we have said that it is impossible to tell a benign from a malignant tumor even with the tumor in your hand at operation. We must present the pathologist with the entire tumor. This should be done while the abdomen is opened for the true pathological nature cannot be known until the tumor is removed and its interior inspected.

There is no problem in diagnosis when there are papillary excrescences on the external surface or the tumor is fixed to adjacent organs. With this in mind there is one basic move which is mandatory, namely that all tumors, whether they be solid or cystic, should be sectioned in the operating room. We all know this but too frequently it is not done. In far too many instances only the obviously involved ovary is removed. This is particularly true in the 30 to 40 age group where we want to be conservative if possible.

The character of the fluid content provides the clue if it is a cystic tumor. Clear fluid means that this is a serous cystadenoma which may be benign or malignant. If it is malignant it has five times the malignant potential of a pseudomucinous tumor. Papillary cyst adenocarcinomas occur bilaterally at any age and the results of treatment are appreciably worse.

The pseudomucinous cyst contains a gelatinous fluid. The growth pattern is not unlike the papillary cystadenocarcinoma but its biological behaviour is different and much less lethal. If their growth pattern is confined to the interior or there is minimal spread to the adjacent peritoneum one might be willing to take a calculated risk, in a young patient, and remove only the tumor on the affected side.

It is a well established fact that the more solid the tumor the more likely it is that the tumor will be malignant. We become suspicious if solid portions appear in the wall of a multiloculated cystic tumor that contains papillary excrescences. Biopsy solid portions.

Of all the solid tumors only the thecoma and the fibroma are benign. The appearance of the cut surface of the benign tumors is highly characteristic for it closely resembles the benign fibroid. Any departure from this feature should be regarded with grave suspicion.

The basic treatment for cancer of the ovary is surgery which calls for the total removal of the uterus and both tubes and ovaries, combined with immediate or subsequent chemotherapy and/or irradiation. It may not be necessary to remove omentum. Don't dissect regional nodes. The spread is much more likely to be to the chain of retroperitoneal nodes along the aorta, the renal veins and the celiac axis. Too often both ovaries are removed and the uterus is left in place. This is unwise for there is too much lymphatic communication between the involved ovary, the tube, the uterine musculature and the opposite ovary. It is Kottmeier's habit to leave the uterus in place to serve as a site for the introduction of radium sources but there has been little enthusiasm for it in the United States.

The other ovary should be removed even though it outwardly appears normal. Many neoplasms do arise in both ovaries and we have maintained that metastases may have taken place through lymphatic channels.

Remove the omentum if tumor is present in it or there is wide intra abdominal spread. The proponents for leaving it point out that the patient may be more inclined to develop intestinal obstruction if it is removed. It is impossible to show any increase in longevity from omentectomy.

Let us now discuss staging and histopathology and their relation to therapy.

Clinical staging is certainly not the only factor in prognosis. Not enough attention had been paid to histology. Many tumors with low malignant potential were included among the more invasive cancers because they (a) produced papillary growth, (b) created ascites, and (c) occasionally metastasized. In some of these tumors epithelial proliferation elements are present. They differ from established cancer only in the most important factor — invasion is lacking. The growth pattern of mucinous and endometrial tumors tend to be fairly slow and more are in Stage I where the tumor is confined to the ovary. In contrast the life history of papillary serous tumors is more aggressive. Only 21 percent of these tumors are limited to the ovary. This influences the chances of survival materially. When the tumor has spread beyond the ovary only 20 percent of the papillary serous tumors survive. Contrast this with the 51

percent of endometrial tumors who survive 5 or more years. Papillary excrescences on the surface of the ovary may possibly not carry the gloomy prognosis we have come to predict when they are seen in serous tumors.

Proper attention must also be given to histopathology. The most important factor in evaluating prognosis seems to be (a) spread beyond the ovary, (b) whether or not both ovaries are involved. The presence or absence of ascites seems to have little impact on survival.

If the cancer is confined to one ovary you may expect to have 65 percent alive at 5 years. If both ovaries are involved but the tumor is confined to them 36 percent will survive 5 years. There is an obvious change for the worse when both ovaries contain tumor regardless of whether or not (a) the growth is fixed to the surrounding tissues without obvious metastases, or (b) metastases are grossly evident, (c) when the tumor involves both ovaries, and metastases are widespread the prognosis is poor at 7 percent.

There is discrepancy in survival figures in Stage II where the cancer has extended to the uterus and pelvic tissues. It is here that the histological classification is so important.

What about conservative surgery? There is a place for it in the younger woman who either wants to have a child or feels that her family is not complete and one would like to preserve her menstrual function. There is no place for conservatism in a woman beyond her reproductive years whether the neoplasm is benign or malignant. The treatment then is hysterectomy with removal of the opposite ovary.

You would like to save the uterus and other ovary in the young patient. Simple oophorectomy is indicated only (a) when the growth pattern of the neoplasm is usually unilateral, or (b) when the tumor has a low malignant potential and there is no obvious area of invasion. One will then choose to do a simple oophorectomy if the histology of the tumor was either mucinous or endometrioid and it was important to the young patient to preserve her menstrual function. The danger lies in the group of serous tumors which are bilateral 60 percent of the time in contrast to the pseudomucinous tumors where it can be expected in 20 percent and the endometrioid where it occurs 30 percent of the time. The serous tumors grow more rapidly as shown by the fact that over 50 percent are in the advanced category when first seen. They are also more lethal. When confined to the ovary 83 percent of the mucinous and 81 percent of the endometrioid tumors will be alive at 5 years. This is in sharp

contrast to the serous cystadenocarcinomas where only 40 percent survive 5 years.

Too often the surgeon simply palpates the opposite ovary without taking a biopsy if he elects not to remove it.

We then return to the question of whether or not one can reasonably be conservative and leave the opposite ovary. If the tumor is pseudomucinous and there are rare microscopic foci of malignancy it may be all right to be conservative. It is less true of endometrioid tumors.

If the pathologist is unable or unwilling to make a diagnosis and there is no gross evidence of extension beyond the capsule the surgeon may take a calculated risk and leave the uterus and opposite ovary. When he takes the risk he gambles that (a) the evidence of malignant change is minimal, and (b) the pathology is such that further spread is unlikely and the retained ovary is unlikely to become involved; (c) no other neoplasia, either benign or malignant, is likely to appear in the ovary at a later date. The risk of this happening is about the same as the likelihood of developing carcinoma of the ovary anyhow. Randall found 7 percent of 310 developed another tumor and one third of these were malignant. The chances of another neoplasm appearing in the retained ovary will be less than this if the opposite ovary is biopsied. If the surgeon is unwilling to take the gamble he should do a simple oophorectomy and wait for the permanent sections to make the definite diagnosis.

After conservatism, if you get malignant report, the surgeon may then decide whether or not to re-operate and remove the other ovary and the uterus. If the report indicates that the histology is either pseudomucinous or endometrioid and it is confined to the ovary the surgeon may elect to take a calculated risk and not operate at all. This would not be true if the pathology reveals a serous cystadenocarcinoma. Kottmeier, in this situation, recommends 4-5000 R of external x-ray therapy directed to the pelvis followed by re-exploration to remove the uterus, and other ovary. The patient does not have a choice if the tumor is papillary serous in type. She should have radical treatment. If the tumor is endometrioid or mesonephric the patient can be given a choice if she is young and wants to save her reproductive capacity.

If the cancer is no longer confined to the ovary, the patient should be subjected to exploration even though there is (1) extensive induration and palpable tumor in the cul de sac, or (2) when there are large masses within the abdominal cavity. The primary aim should be to

remove all tumor but in many instances this is neither feasible nor justifiable. The measure of success will depend on how successful you have been in excising bulk tumor. In many instances the peritoneal extensions simply represent papillary tumor that has heaped up on the peritoneum without invading the peritoneum and the tissue behind it. It contains more fibrous tissue than cells. This is particularly true of endometrioid tumors. Frequently the peritoneal extensions can be removed without danger to the patient or risk of interfering with the function of the abdominal viscera. One is justified in removing as much tumor as possible even though you know you are leaving tumor behind. This would be unthinkable for any other type of tumor except ovarian cancer which has such variable characteristics based on its capacity for multipotential growth. Mature judgment is needed to decide how much of the widely disseminated tumor should be removed. It is an extremely rare case that will benefit from either partial or total exenteration. It is of basic importance that the primary site be removed.

When the surgeon has removed as much of the ovarian cancer as he feels justified in doing and the primary site has been removed he may then add supplementary therapy in the form of external radiation therapy, chemotherapy or at times a combination of the two. As a final recourse he may elect to take a second look after completing the supplementary therapy.

Recently the technique of giving external radiation has undergone a change in the method of administering it to patients with ovarian disease which cannot be removed in its entirety at the time of surgical intervention. Originally the so-called trips technique was given by Cobalt 60, but it is now given by megavolt machines as well. 2.5 cm. areas are marked out on the skin both front and back. Daily treatments are given through these areas by alternating front and back, with one additional strip added each day. By moving the strips each day a greater biological effect can be obtained in a shorter period of time. The surrounding tissues receive less radiation and the side effects are minimized and weight is maintained. The kidneys and liver are protected with lead shields. A total tumor dose of 2500 - 2700 is given. The results improve if pelvic irradiation is given after completion of the abdominal exposure.

The important factors in achieving results are (a) the histology, (b) the initial amount of tumor the patient had, and (c) the extent of the residual carcinoma. Delcos, who has had the largest experience with this form of therapy is encouraged by the results

in both stages II and III, particularly when radiation is given to both abdomen and pelvis. There are twice as many survivors when the strip technique is used in patients who have palpable disease in the stage II category than was possible after the conventional methods of external radiation. The results are even more dramatic in stage III. By conventional methods there were no survivors as against 7 of 19 when the strip technique was used. It does depend somewhat upon the amount of tumor remaining after surgical excision. Delcos makes the point that the best results are obtained when as much tumor as possible is removed at operation. When the masses are too large it may be wise to give chemotherapy prior to the radiation. Rutledge, from the same clinic, does this routinely on the theory that irradiation will have less tumor to deal with if the tumor responds to chemotherapy.

It is difficult to evaluate the results of chemotherapy for there is considerable difference of opinion as to what definition is given to (a) the term objective response, (b) how long the remission should last before calling it a favorable response, and (c) whether the chemotherapy is given before or after radiation treatment and (d) the nature of the histology. Frick points out that the only successful agents have been the alkylating agents such as nitrogen mustard, chlorambucil, thiotepe, cytoxan and alkeran. In his opinion no one drug has been notably more effective than any other. Some of the drugs such as chlorambucil and alkeran can be taken orally while others have to be given by the intravenous route. Many of the patients have marked subjective improvement even though the effect on the tumor is not particularly noticeable. Using leukeran Rutledge obtained a 50 percent objective improvement when the drug was given for 3 months. To be considered as a success the tumor had to regress by 50 percent and the abdominal and pleural effusions had to disappear. Masterson obtained a similar response with chlorambucil as Decker did with cytoxan. There is always considerable question of how long the chemotherapy should be given to sustain a remission.

Frick points out that to date there are no 5 year reports following the use of the alkylating agents for advanced ovarian cancer. Actually Frick was unable

to show any overall improvement in survival where chemotherapy was used for advanced cancer over the results obtained by surgery alone or in combination with x-ray.

What about a second look? There has been some mild degree of enthusiasm for re-exploration 3 or 4 months after irradiation has been completed. The rationale appears to be that at times the tumor which appears to be fixed when exploration is done became free under the influence of irradiation and chemotherapy. It is always a question of what should be done when the tumor is solidly fixed to the colon, small intestine or bladder. A resection is reasonable if it can be done on bloc and there is no evidence of additional spread such as seeding on the small bowel, mesentery or peritoneum of the lateral gutters. This is particularly true of the mucinous tumors for they do not respond very well to irradiation. Actually excision of tumor adherent to bowel is not very rewarding for the majority are dead in 6 months.

In conclusion — the best chance we have of improving our salvage in ovarian carcinoma is earlier diagnosis. While the histology is an important consideration it is obvious that we can expect a more favorable response to the various modes of therapy if the tumor is confined to the ovary or the pelvic areas immediately adjacent to it.

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TETANOS EN PUERTO RICO

A través de los años, varios estudios han demostrado una sustancial disminución en la incidencia de tétanos (1-6) en nuestra Isla, especialmente en los años 1965-66 y 1966-67. Sin embargo, como lo demuestra el reciente estudio realizado en el Area Sur de Puerto Rico (7), el problema dista de haber sido resuelto.

En vista de que la inmunización activa contra el tétanos es especialmente efectiva y de que la inmunización pasiva con globulina humana antitetánica ha simplificado extraordinariamente su prevención, la pregunta que debemos hacernos es: ¿Por qué no desaparece una enfermedad que sí puede desaparecer?

Es evidente por el trabajo de Ratner y coautores (6) y el publicado en esta misma edición que el por ciento de vacunados, aunque alcanzó el 68.3 por ciento de nuestra población en los años de la vacunación en masa, dejó dos grupos, los infantes y los adultos sobre 40 años, sin protección adecuada. De ahí se explica el que la enfermedad se haya convertido en una que primordialmente afecta a adultos, el grupo menos protegido por la vacunación.

Para el desarrollo de un programa más efectivo se requiere la coordinación de diversas agencias que laboren en la prevención del tétanos a base del siguiente esquema:

1. La vacunación de la población infantil en los dos primeros años de vida debe ser extendida, y continuada como una política básica de la salud pública y de la medicina privada.
2. La vacunación a nivel escolar de los niños no vacunados previamente y la revacunación de los ya vacunados debe ser coordinada entre los organismos de salud y los organismos educativos.
3. La revacunación (o una vacunación completa en los casos que sea necesario) de la fuerza trabajadora debe ser instrumentada al pasar el trabajador a quedar bajo la protección del Fondo de Seguro del Estado.
4. La posibilidad de vacunar a las mujeres embarazadas debe ser estudiada por los grupos médicos que practican la obstetricia.
5. La profilaxis pasiva debe ser seguida en todos los casos por inmunización activa, sustituyendo el suero antitetánico de origen equino por globulina humana.

En el plano conceptual es propio recordar que a pesar de que la enfermedad puede desaparecer, la bacteria estará permanentemente presente en nuestro ambiente. Si estamos conscientes de esto y de la necesidad de mantener un programa permanente de prevención habremos dado un importante paso en el objetivo final: el control total de esta terrible enfermedad.

Héctor F. Rodríguez, MD
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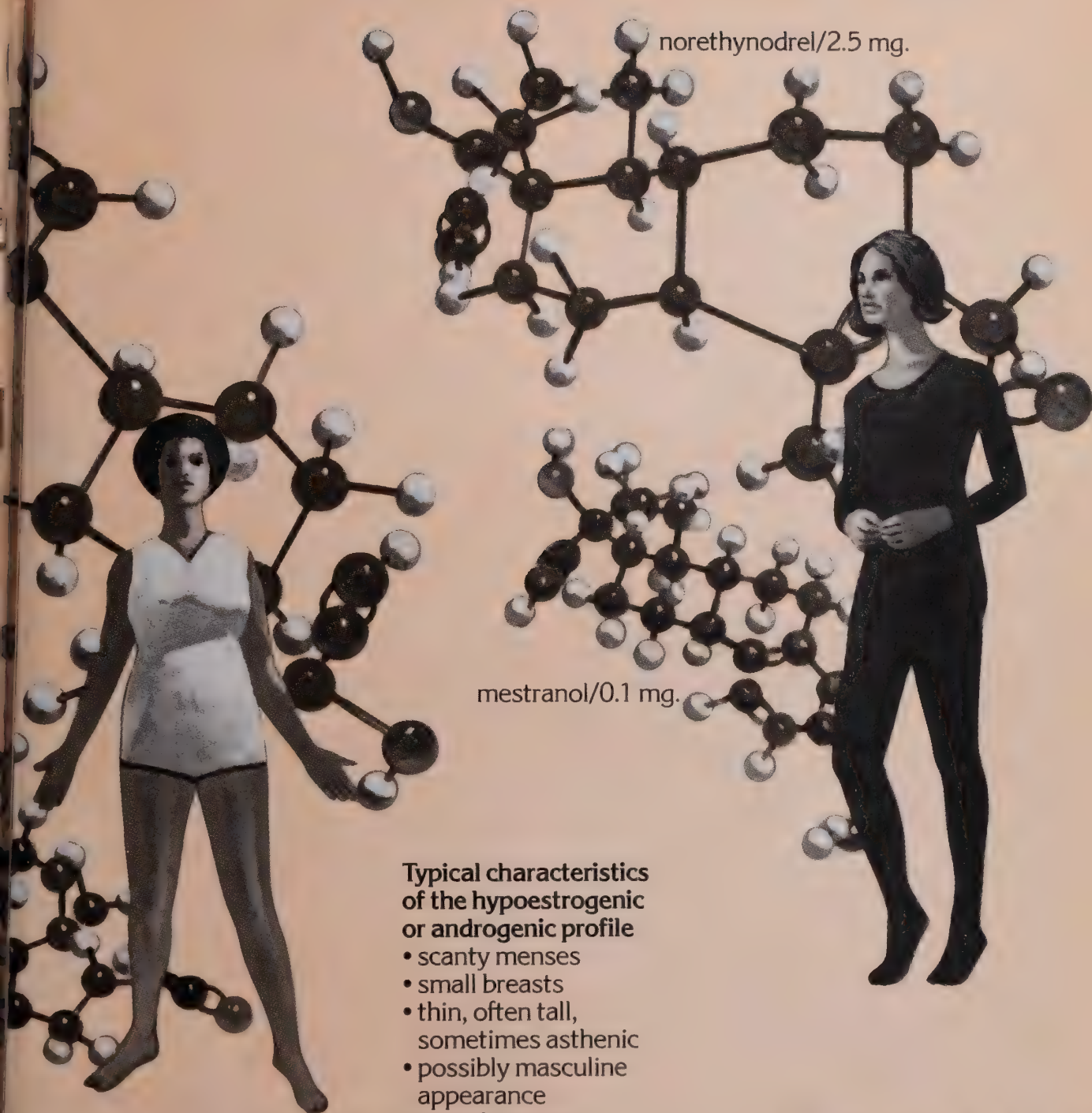
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- scanty menses
- small breasts
- thin, often tall,
sometimes asthenic
- possibly masculine
appearance
- acne, hirsutism
- low sexual motivation
- thin vaginal lining,
tendency to vaginitis
and dyspareunia

This pill has a relatively
weak and unique* progestogen
with inherent estrogenicity.
Clinically, just as in animal
studies, it appears not to
possess antiestrogenic and
androgenic activity.

Enovid-E®

Available in 20- and 21-pill schedules
Each tablet contains: norethynodrel
2.5 mg./mestranol 0.1 mg.

a clear choice for women
when estrogen dominance
and no androgenic activity
are preferred

*Of all the progestogens, norethynodrel
most resembles the molecular structure of
the estrogens. It has the weakest proges-
tational activity of any progestogen in a
combination pill.

Ovulen®

Each white tablet contains:
ethynodiol diacetate 1 mg./mestranol 0.1 mg.

Each pink tablet in Ovulen-28® and Demulen-28® is a placebo, containing no active ingredients.

Actions—Ovulen and Demulen act to prevent ovulation by inhibiting the output of gonadotropins from the pituitary gland. Ovulen and Demulen depress the output of both the follicle-stimulating hormone (FSH) and the luteinizing hormone (LH).

Special note—Oral contraceptives have been marketed in the United States since 1960. Reported pregnancy rates vary from product to product. The effectiveness of the sequential products appears to be somewhat lower than that of the combination products. Both types provide almost completely effective contraception.

An increased risk of thromboembolic disease associated with the use of hormonal contraceptives has now been shown in studies conducted in both Great Britain and the United States. Other risks, such as those of elevated blood pressure, liver disease and reduced tolerance to carbohydrates, have not been quantitated with precision.

Long-term administration of both natural and synthetic estrogens in subprimate animal species in multiples of the human dose increases the frequency of some animal carcinomas. These data cannot be transposed directly to man. The possible carcinogenicity due to the estrogens can be neither affirmed nor refuted at this time. Close clinical surveillance of all women taking oral contraceptives must be continued.

Indication—Ovulen and Demulen are indicated for oral contraception.

Contraindications—Patients with thrombophlebitis, thromboembolic disorders, cerebral apoplexy or a past history of these conditions, markedly impaired liver function, known or suspected carcinoma of the breast, known or suspected estrogen-dependent neoplasia and undiagnosed abnormal genital bleeding.

Warnings—The physician should be alert to the earliest manifestations of thrombotic disorders (thrombophlebitis, cerebrovascular disorders, pulmonary embolism and retinal thrombosis). Should any of these occur or be suspected the drug should be discontinued immediately.

Retrospective studies of morbidity and mortality conducted in Great Britain and studies of morbidity in the United States have shown a statistically significant association between thrombophlebitis, pulmonary embolism, and cerebral thrombosis and embolism and the use of oral contraceptives. There have been three principal studies in Britain¹⁻³ leading to this conclusion, and one⁴ in this country. The estimate of the relative risk of thromboembolism in the study by Vessey and Doll³ was about sevenfold, while Sartwell and associates⁴ in the United States found a relative risk of 4.4, meaning that the users are several times as likely to undergo thromboembolic disease without evident cause as nonusers. The American study also indicated that the risk did not persist after discontinuation of administration and that it was not enhanced by long-continued administration. The American study was not designed to evaluate a difference between products. However, the study suggested that there might be an increased risk of thromboembolic disease in users of sequential products. This risk cannot be quantitated, and further studies to confirm this finding are desirable.

Discontinue medication pending examination if there is sudden partial or complete loss of vision, or if there is a sudden onset of proptosis, diplopia or migraine. If examination reveals papilledema or retinal vascular lesions medication should be withdrawn.

Since the safety of Ovulen and Demulen in pregnancy has not been demonstrated, it is recommended that for any patient who has missed two consecutive periods pregnancy should be ruled out before continuing the contraceptive regimen. If the patient has not adhered to the prescribed schedule the possibility of pregnancy should be considered at the time of the first missed period.

A small fraction of the hormonal agents in oral contraceptives has been identified in the milk of mothers receiving these drugs. The long-range effect to the nursing infant cannot be determined at this time.

Precautions—The pretreatment and periodic physical examinations should include special reference to the breasts and pelvic organs, including a Papanicolaou smear since estrogens have been known to produce tumors, some of them malignant, in five species of subprimate animals. Endocrine and possibly liver function tests may be affected by treatment with Ovulen or Demulen. Therefore, if such tests are abnormal in a patient taking Ovulen or Demulen, it is recommended that they be repeated after the drug has been withdrawn for two months. Under the influence of progestogen-estrogen preparations pre-existing uterine fibromyomas may increase in size. Because these agents may cause some degree of fluid retention, conditions which might be influenced by this factor, such as epilepsy, migraine, asthma, cardiac or renal dysfunction, require careful observation. In breakthrough bleeding, and in all cases of irregular bleeding per vaginam, nonfunctional causes should be borne in mind. In undiagnosed bleeding per vaginam adequate diagnostic measures are indicated. Patients with a history of psychic depression should be carefully observed and the drug discontinued if the depression recurs to a serious degree. Any possible

Demulen®

Each white tablet contains:
ethynodiol diacetate 1 mg./ethinyl estradiol 50 mcg.

influence of prolonged Ovulen or Demulen therapy on pituitary, ovarian, adrenal, hepatic or uterine function awaits further study. A decrease in glucose tolerance has been observed in a significant percentage of patients on oral contraceptives. The mechanism of this decrease is obscure. For this reason, diabetic patients should be carefully observed while receiving Ovulen or Demulen therapy. The age of the patient constitutes no absolute limiting factor, although treatment with Ovulen or Demulen may mask the onset of the climacteric. The pathologist should be advised of Ovulen or Demulen therapy when relevant specimens are submitted. Susceptible women may experience an increase in blood pressure following administration of contraceptive steroids.

Adverse reactions observed in patients receiving oral contraceptives—A statistically significant association has been demonstrated between use of oral contraceptives and the following serious adverse reactions: thrombophlebitis, pulmonary embolism and cerebral thrombosis.

Although available evidence is suggestive of an association, such a relationship has been neither confirmed nor refuted for the following serious adverse reactions: neuro-ocular lesions, e.g., retinal thrombosis and optic neuritis.

The following adverse reactions are known to occur in patients receiving oral contraceptives: nausea, vomiting, gastrointestinal symptoms (such as abdominal cramps and bloating), breakthrough bleeding, spotting, change in menstrual flow, amenorrhea during and after treatment, edema, chloasma or melasma, breast changes (tenderness, enlargement and secretion), change in weight (increase or decrease), changes in cervical erosion and cervical secretions, suppression of lactation when given immediately post partum, cholestatic jaundice, migraine, rash (allergic), rise in blood pressure in susceptible individuals and mental depression.

Although the following adverse reactions have been reported in users of oral contraceptives, an association has been neither confirmed nor refuted: anovulation post treatment, premenstrual-like syndrome, changes in libido, changes in appetite, cystitis-like syndrome, headache, nervousness, dizziness, fatigue, backache, hirsutism, loss of scalp hair, erythema multiforme, erythema nodosum, hemorrhagic eruption and itching.

The following laboratory results may be altered by the use of oral contraceptives: hepatic function: increased sulfobromophthalein retention and other tests; coagulation tests: increase in prothrombin, Factors VII, VIII, IX and X; thyroid function: increase in PBI and butanol extractable protein bound iodine, and decrease in T³ uptake values; metyrapone test and pregnanediol determination.

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norethynodrel 2.5 mg./mestranol 0.1 mg.

Actions—Enovid-E acts to prevent ovulation by inhibiting the output of gonadotropins from the pituitary gland. Enovid-E depresses the output of both the follicle-stimulating hormone (FSH) and the luteinizing hormone (LH).

Indication—Enovid-E is indicated for oral contraception.

The *Special Note*, *Contraindications*, *Warnings*, *Precautions* and *Adverse Reactions* listed above for Ovulen and Demulen are applicable to Enovid-E and should be observed when prescribing Enovid-E.

Enovid-E®

brand of norethynodrel with mestranol

SEARLE

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Division of G. D. Searle & Co.
Box 5110, Chicago, Illinois 60680
Where "The Pill" Began

SALE OR DISPOSITION OF A MEDICAL PRACTICE

(Prepared by The Office of the General Counsel of the American Medical Association)

THE PHYSICIAN'S WILL

There are many personal reasons for a physician to have a Last Will and Testament. A Will transfers a person's property upon his death to those people for whom he wishes to provide a benefit. Properly drawn, a Will can not only transfer one's property upon his death, but can also transfer it under circumstances which provide adequate protection for those beneficiaries who may need some type of protection. Additionally, the Will can transfer one's property in such a way as to obtain the most favorable tax treatment. A Will also permits the testator (the person whose Will it is) to name a guardian for any minor children who may survive the testator and his or her spouse. A Will can also provide for any number of contingencies which may occur.

Of course, every physician should have a Will, but for the physician who is a sole practitioner, a Last Will and Testament has added significance. The disposition of his practice cannot be efficiently and effectively accomplished without a properly drafted Will. Unlike his colleagues who practice in a partnership or a professional corporation, he does not have the opportunity to enter into a "Buy and Sell" agreement with his partners. Therefore, his Will must contain the necessary authorization to permit his family to sell the practice. His Will must contain what is known as a "Power of Sale" provision, which authorizes the Executor of the Will to sell or dispose of all or any part of the property comprising his estate, without the necessity of having a Court approve the sale. Without this provision in a Will, the law limits the occasions when property may be sold by an Executor, and requires Court approval of any proposed sale by the Executor. The procedural and substantive difficulties involved in obtaining Court approval, and the resultant delays which would be

involved could have a disastrous effect on the terms of any proposed sale.

The importance of a Will should be obvious, but it should be equally apparent that the Will should be prepared only by an attorney and only after he has been apprised of all of the facts relating to the physician's family, his practice, the other aspects of his estate, and the particular wishes and desires of the physician. The attorney will want to evaluate all of these factors and perhaps suggest an "estate plan" which would also take into consideration the physician's life insurance, and any joint tenancies which the physician may have created. These latter elements are not affected by a Will, but may have a profound effect on the tax consequences of the estate. Accordingly, the attorney may suggest some type of trust arrangement, either separate from the Will or as a part of the Will.

One last item on the physician's Will, and that is, that the Will, or the "estate plan" should never be considered to be final. It should be reviewed and undated as often as circumstances warrant a change. Births, deaths and marriages in the family are all occasions which make it both wise and appropriate to review one's own circumstances. So also is the occasion when the physician takes on a partner, or retires from practice. The opportunity to review, and to provide more currently effective protection for one's family, should not be postponed. The ease and efficiency with which your estate can be administered is a kindness only you can give to your family.

CONCLUSION

One final suggestion may be the most helpful of all, and that is to consult with the local medical society. They will probably be able to offer help and counsel every step of the way, and offer valuable suggestions to avoid pitfalls that could only be discovered by someone who has experienced them. The physician who is

retiring from active practice may find the advice and experience of his colleagues most beneficial to him, and of course, he will want to arrange to maintain his membership and participation in the medical society during his retirement.

For the family of the deceased physician, the local medical society can usually offer sure, specific advice

and sometimes actual tangible assistance on the multitude of problems which this paper has merely listed. The physician who is seeking to purchase a medical practice usually consults the local medical society in the community. Isn't this is a good starting place for someone who needs to sell a medical practice?

NOTICIAS

FROM THE AMERICAN MEDICAL ASSOCIATION:

A session will be given at the AMA annual convention on "Rehabilitating the Stroke Patient in the Geriatric Day Hospital". This session will be held in the Ballroom of the Sheraton Hotel, New York City, on Tuesday, June 26, 1973, from 9 am to 12 noon.

The staff of the Day Hospital at the Burke Rehabilitation Center, White Plains, New York, will present a play in two acts. The focus of the drama will be on the psychosocial problems facing a stroke patient and his family. It will portray episodes in the rehabilitative process within a day hospital setting. A series of vignettes will highlight the treatment team in action.

Live dramatization will include the interrelated roles of the disciplines of medicine, nursing, physical therapy, occupational therapy, psychology, social service, and speech therapy as they work with the patient and family members toward the goal of maximum function and adjustment for the patient.

Attendance at the Seminar is acceptable for:

Category No. 2, American Medical Association
Physician's Recognition Award

American Academy of Family Physicians
(credit applied for)

Continuing education credit by State Board of Examiners
for Nursing Home Administrators where applicable.

There is no registration fee and the session is open to all health professionals.

CIGARETS BLAMED FOR RISE IN FATAL HEART ATTACKS AMONG WOMEN

Chicago — Heavy cigaret smoking among women is blamed for a marked increase in sudden death from coronary heart disease among the feminine sex in a report in the current (May 14) issue of the Journal of the American Medical Association.

The report, from Brookdale Hospital Medical Center, Brooklyn, and Westchester County Medical Examiner's Office, Valhalla, N. Y., states that women are gaining steadily on men in frequency of sudden death from heart attack.

In the 1950s there were 12 sudden deaths in men from coronary heart disease (CHD) for each one in women. In the late 1960s, the ratio had dropped to four to one. This shift has been associated with an increase in heavy cigaret smoking among women, the report says.

The study also shows that heavy cigaret smoking may cut a woman's life span as much as 19 years. The mean age for women dying suddenly of heart attack was 67 in the non-smoker, 55 in the light smoker and 48 in the heavy smoker.

SIMPLER RABIES VACCINE SUCCESSFUL IN HUMANS

Chicago — Successful human test of a new and much

safer rabies vaccine is reported in the current (May 21) issue of the Journal of the American Medical Association.

The vaccine uses rabies virus grown in human diploid cell cultures rather than in cultures of duck embryo, the common source of the vaccine now in general use. The human diploid cell nutrient is also used in a new version of polio vaccine released last year.

Antibody titers (the body's own defense mechanism against the rabies virus) after two inoculations of the new vaccine were similar to those previously reported after 14 inoculations of duck embryo vaccine, the researchers say.

Also, only minimal local reactions and no general reactions to the new vaccine were noted. Vigorous and uncomfortable reactions to the duck embryo vaccine are common. The latter also requires a large number of injections to induce the body to build its defenses against the rabies virus, while the new vaccine requires only two or three doses.

DRUG-RESISTANT TYPHOID FEVER STRAIN REPORTED IN MEXICO

Chicago — Travelers returning from Mexico are bringing back cases of typhoid fever that resist the commonly used typhoid drugs, says a report in the current (May 7) issue of the Journal of the American Medical Association.

At least seven cases of typhoid fever caused by chloramphenicol-resistant strains of microbes have been imported into the United States from northern and central Mexico, where typhoid is now epidemic, the report says.

Chloramphenicol is generally accepted as the medication of choice for treatment of typhoid. Other drugs sometimes used are streptomycin sulfate, tetracycline and sulfonamides. These also do not affect the resistant microbes.

The typhoid strains cause drug resistance similar to that encountered in the last few years in severe dysentery in some Latin American countries. The drug-resistant dysentery, also has been found in the United States, apparently imported via pet monkeys from Nicaragua, the researchers state.

TEACHING 2-YEAR-OLDS TO SWIM HELD OF DOUBTFUL SAFETY VALUE

Chicago — Teaching very young children to swim is of doubtful value in protecting them from drowning, says an article in the current (May) issue of American Journal of Diseases of Children, a publication of the American Medical Association.

Even if the 2 or 3-year-olds learn to "swim", the level of skill is inadequate to cope with most accidents of falling in the water, says Albert B. Craig, M. D., a physiology professor at the University of Rochester School of Medicine and Dentistry, Rochester, N. Y.

SEMINAR IN PEDIATRIC NEPHROLOGY: CURRENT CON-

the bare facts.

in many dermatoses* the less they wear,
the more they need...

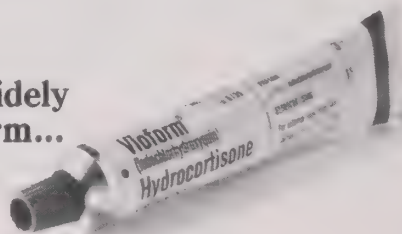
Vioform[®]-Hydrocortisone (iodochlorhydroxyquin and hydrocortisone)

antifungal • antibacterial • anti-inflammatory • antipruritic

Some styles don't leave much to the imagination. And don't provide much cover for common dermatoses, either. Just like plain topical steroids. If the lesion has become infected with fungi or bacteria, plain topical steroids are ordinarily not recommended as sole therapy. Vioform-Hydrocortisone, on the other hand, provides the kind of comprehensive therapy these dermatoses may require. It not only supplies the anti-inflammatory and antipruritic actions of hydrocortisone...but also adds the antibacterial and antifungal actions of Vioform.

*This drug has been evaluated as possibly effective for these indications. See brief prescribing information.

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the most widely
prescribed form...
20 Gm cream**





Vioform®-Hydrocortisone
(iodochlorhydroxyquin and hydrocortisone)

INDICATIONS

Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, FDA has classified the indications as follows:

"Possibly" effective: Contact or atopic dermatitis; impetiginized eczema; nummular eczema; infantile eczema; endogenous chronic infectious dermatitis; stasis dermatitis; pyoderma; nuchal eczema and chronic eczematoid otitis externa; acne urticata; localized or disseminated neurodermatitis; lichen simplex chronicus; anogenital pruritus (vulvae, scroti, ani); folliculitis; bacterial dermatoses; mycotic dermatoses such as tinea (capitis, cruris, corporis, pedis); moniliasis; intertrigo.

Final classification of the less-than-effective indications requires further investigation.

CONTRAINDICATIONS

Hypersensitivity to Vioform-Hydrocortisone, or any of its ingredients or related compounds; lesions of the eye; tuberculosis of the skin; most viral skin lesions (including herpes simplex, vaccinia, and varicella).

WARNINGS

This product is not for ophthalmic use.

In the presence of systemic infections, appropriate systemic antibiotics should be used.

Usage in Pregnancy

Although topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use in pregnant females has not been established. Therefore, they should not be used extensively on pregnant patients in large amounts or for prolonged periods of time.

PRECAUTIONS

May prove irritating to sensitized skin in rare cases. If this occurs, discontinue therapy. May stain.

If used under occlusive dressings or for a prolonged period, watch for signs of pituitary-adrenal axis suppression.

May interfere with thyroid function tests. Wait at least one month after discontinuance of therapy before performing these tests. The ferric chloride test for phenylketonuria (PKU) can yield a false-positive result if Vioform is present in the diaper or urine.

Prolonged use may result in overgrowth of unsusceptible organisms requiring appropriate therapy.

ADVERSE REACTIONS

Few reports include: Hypersensitivity, local burning, irritation, pruritus. Discontinue if untoward reaction occurs. Rarely, topical corticosteroids may cause striae at site of application when used for long periods in intertriginous areas.

DOSAGE

Apply a thin layer to affected areas 3 or 4 times daily.

HOW SUPPLIED

Cream, 3% Iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearyl alcohol, spermaceti, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of 5 and 20 Gm. *Ointment*, 3% Iodochlorhydroxyquin and 1% hydrocortisone in a petrolatum base; tubes of 5 and 20 Gm. *Lotion*, 3% Iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearic acid, cetyl alcohol, lanolin, propylene glycol, sorbitan trioleate, polysorbate 60, triethanolamine, methylparaben, propylparaben, and perfume Flora in water; plastic squeeze bottles of 15 ml. *Mild Cream*, 3% Iodochlorhydroxyquin and 0.5% hydrocortisone in a water-washable base containing stearyl alcohol, spermaceti, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of ½ and 1 ounce. *Mild Ointment*, 3% Iodochlorhydroxyquin and 0.5% hydrocortisone in a petrolatum base; tubes of ½ and 1 ounce.

Consult complete product literature before prescribing.

CIBA Pharmaceutical Company
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C I B A

CEPTS IN DIAGNOSIS AND MANAGEMENT

- Presented by: Division of Pediatric Nephrology, Department of Pediatrics
University of Miami School of Medicine
Miami, Florida
- Director: José Strauss, MD, Professor and Chief,
Division of Pediatric Nephrology
- Location of Course: Eden Roc Hotel
Miami Beach, Florida
- Dates: January 2-5, 1974
- Tuition: \$125; Residents and Fellows \$50 with
certification of Chief of Service
- Description: A comprehensive review of major problems in Pediatric Nephrology. Pathogenesis, pathology, clinico-pathological correlations, functional derangements and treatment of glomerulopathies, structural defects and infections, and chronic uremia will be emphasized.
- Inquiries: Division of Continuing Education, University of Miami School of Medicine, P. O. Box 875 Biscayne Annex, Miami, Florida 33152 (Tel. A/C 305, 350-6716).

METHAQUALONE:

SCHEDULE III VERSUS SCHEDULE II

THE STATUTE:

The Controlled Substances Act of 1970 established five schedules, each representing a separate level of abuse potential and varying regulatory requirements and penalties. Schedule I contains illegal drugs such as heroin and LSD. Schedule V is the least severe classification and includes Rorer's Parepectolin[®], an OTC antidiarrheal containing paregoric.

THE ISSUE:

Rorer has recommended that methaqualone be placed in Schedule III along with similar products like glutethimide. The federal Bureau of Narcotics and Dangerous Drugs has recommended that methaqualone be classified in Schedule II along with raw opium, methadone and amphetamines.

THE PROFESSIONAL ISSUE:

No one objects to reasonable regulations and procedures that will help control the diversion of legal drugs into illegal channels. The American prescription system, itself, is designed to provide such control. But in this age of drug abuse and related social problems there is a frightening move toward police control without regard for the patients who need drugs for legitimate medical uses. Our government agencies are asking for all the power they can get.

From a medical and scientific point of view there is no justification for placing methaqualone in Schedule II while barbiturates and glutethimide remain in Schedule III. No reliable evidence has been presented that would indicate methaqualone causes severe psychological or physical dependence, as required for placement in Schedule II.

If the BNDD is successful in placing more and more drugs in Schedules that are unduly restricting, we will have a prescription system that is burdensome to the physician, expensive for the patients and impractical in distribution channels. Rorer believes that it is time to draw the line and demand that the regulations be interpreted as they are written. The practice of medicine is complicated enough without additional political interference.

WRITE A LETTER:

As a prescriber of methaqualone if you also think Schedule II is too strict you can help immeasurably by sending your comments to the Chief Counsel of the BNDD.

The Reference: *Federal Register*, April 11, 1973.

The Subject: Proposal of the BNDD to place methaqualone in Schedule II of the Controlled Substances Act of 1970.

The Address: All interested persons are invited to submit their comments or objections in writing to:
Office of Chief Counsel
Bureau of Narcotics and Dangerous Drugs
Department of Justice, Room 611
1405 "I" Street, N. W.
Washington, D. C. 20537

The Content of your letter is, of course, up to you. Tell how long you have been prescribing methaqualone, what your professional opinion is regarding its usefulness in your practice, and any particular points you want to make about its safety and efficacy. It is very important to comment about any evidence you have seen of dependency, or lack thereof. It is also important to state your opinion about proposed overregulation of medical practice and the inconvenience and added cost to your patients of Schedule II's restrictions.

Again, we know that methaqualone, like so many other drugs, is being abused. We need added controls. But we need not unduly restrict the prescription system in order to provide added police and regulatory power to combat abuse.

EL INSTITUTO PSIQUIATRICO DE PUERTO RICO ofrece un número limitado de posiciones para residencias en Psiquiatría a tiempo parcial, reconocida por el American Board of Neurology and Psychiatry.

Esta invitación de entrenamiento va dirigida específicamente a compañeros en distintas posiciones y práctica. El entrenamiento les permitirá continuar atendiendo a la población, a su familia y a sus propios compromisos. Al mismo tiempo se preparan sólidamente en la especialidad de la psiquiatría.

El entrenamiento a tiempo parcial conlleva cuatro mañanas: Lunes, Martes, Miércoles y Jueves de 8:00 a 12:00 m. El viernes de 1:00 a 5:00 pm. Incluye asignación parcial de casos hospitalizados en consulta externa y en práctica supervisada. Se extiende por un período de 6 años, aunque sería convertible en residencia (de tiempo completo) según las posibilidades del servicio y el deseo del candidato.

La residencia a tiempo parcial se sufraga en pagos de matrícula anual — pagaderos por semestre adelantado.

Para informes diríjase a: Dr. Víctor Bernal y del Río, Direc-

tor Ejecutivo, Puerto Rico Institute of Psychiatry, Apartado 789, San Juan, Puerto Rico 00919.

OBRAS INCORPORADAS RECIENTEMENTE EN LA BIBLIOTECA DE LA UNIVERSIDAD DE PUERTO RICO, RECINTO DE CIENCIAS MEDICAS (RECENT ACQUISITIONS AT THE LIBRARY OF THE UPR MEDICAL SCIENCES CAMPUS)

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A N U N C I O S

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L I S T A D E A N U N C I A N T E S

1. Burroughs Wellcome — Neosporin
2. Ciba Pharm. — Vioform Hydrocortisone
3. Eaton Labs. — Macrodantin Capsules
4. Geigy Pharm. — Tandearil
5. Ortho — Gravindex
6. Pharmaceutical Manufacturers Assn.
7. Roche — Efudex, Librium, Valium
8. Rorer — Camalox
9. Searle — Demulen, Enovid-E, Ovulen
10. Syntex Labs. — Neo-Mull-Soy
11. Upjohn — Unicap Therapeutic



Julian Katz, M.D.
*Assistant Professor of
Medicine and Director,
Clinical Research Laboratory,
Section of Gastroenterology,
Medical College of Pennsylvania*

Gastrin: an updated look at an important hormone

Early in this century Edkins showed that the intravenous injection of an extract of antral mucosa would stimulate gastric acid secretion. He gave the name gastrin to this proposed hormone. After Komarov substantiated the presence of such a hormone, Gregory and fellow workers isolated, characterized, and synthesized the polypeptide. Gastrin not only has an important influence on acid secretion, but also plays a major role in other gastrointestinal functions.

Structure

Antral gastrin contains 17 amino acids. It is remarkable that a 4 amino acid segment, the carboxyl terminal portion, can reproduce all the activities of which the whole molecule is capable.

Gastrin and feedback mechanism of acid secretion

Gastrin is produced primarily by the mucosal cells in the gastric antrum, the distal non-acid secreting portion of the stomach. The hormone stimulates the parietal cells in the fundus and body of the stomach to produce acid, and a negative feedback mechanism is initiated. Acid bathing the antrum acts directly on the gastrin-producing cell to inhibit release of the hormone.

Gastrin and the lower esophageal sphincter

Contraction of the gastroesophageal sphincter is stimulated by

gastrin. The sphincter muscle is more sensitive to the effects of gastrin than adjacent esophageal muscle. The efficacy of antacid therapy in reflux esophagitis may be due, in part, to the release of antral gastrin. Antacids neutralize gastric acid and raise the pH in the antrum. The gastrin which is then released increases the strength of the sphincter, which acts as a barrier against reflux.

Some other actions of gastrin

Beyond gastrin's prime role as a stimulator of gastric acid production, gastrin also acts on other parts of the G.I. tract. On the stomach, to stimulate (albeit weakly) pepsin production and increase gastric antral motility. On the pancreas, by stimulating enzyme secretion. On the liver, by increasing the flow of bile. On the intestine, by inhibiting absorption of water and electrolytes, and—possibly—increasing motility. And, on the ileocecal sphincter, by relaxing it (contrary to its action on the gastroesophageal sphincter), and perhaps contributing to the gastro-colic reflex.

Excessive gastrin production

It would be expected that if the stomach could not produce acid, gastrin release would continue unabated. Indeed such is the case in pernicious anemia, where there is achlorhydria, and circulating gastrin levels are very high. Alka-

linization of the antrum, vagal stimulation, and mechanical distension of the antrum all provoke gastrin release.

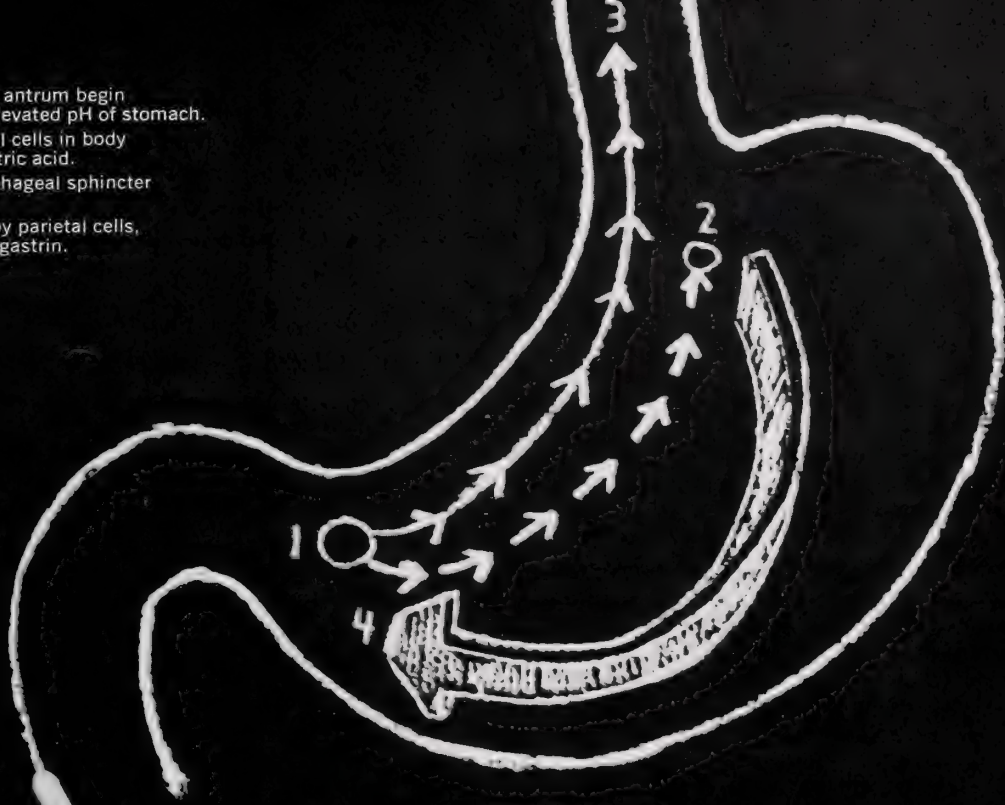
In the Zollinger-Ellison syndrome the radioimmunoassay of gastrin may be the best diagnostic technique. The islet-cell tumor produces large amounts of gastrin, leading to gastric hypersecretion and often intractable ulcer disease. Another situation in which gastrin levels may be high, is when the antrum is retained after gastric resection. Here the antrum is removed from the inhibitory effects of acid, and hypersecretion of gastrin occurs.

Some therapeutic implications

Obviously surgical removal of the antrum will lower gastric secretion as therapy for peptic ulcer disease. But other ways of antagonizing gastrin are being investigated. Some substances have a close structural similarity to the gastrin molecule. For example, cholecystokinin, the intestinal hormone, and caerulein, a material extracted from the skin of amphibians, contain in their structure a sequence of amino acids identical to the active terminal portion of gastrin. These substances are competitive inhibitors of gastric secretion. They combine with the receptor site for acid secretion, cause little stimulation of the receptor, and thus occlude the site.

Keys

1. Gastrin-producing cells in antrum begin secreting in response to elevated pH of stomach.
2. Gastrin stimulates parietal cells in body and fundus to secrete gastric acid.
3. Contraction of gastroesophageal sphincter facilitated by gastrin.
4. Resulting HCl, produced by parietal cells, inhibits further release of gastrin.



CamaloxTM

The pleasant answer to unpleasant problems of hyperacidity

Ever since Camalox was introduced, physicians have been making the discovery that here, indeed, is an antacid that does what an antacid is designed to do.

And does it most agreeably.

It neutralizes excess acid—associated with peptic ulcer, gastritis, esophagitis, hiatal hernia and heartburn.

Fast. And thoroughly.

Consider the patient suffering from hiatal hernia, with accompanying esophageal reflux—it is postulated that the release of gastrin during antacid alkalization of gastric contents may help the gastroesophageal sphincter constrict, thereby helping to stop reflux and subsequent heartburn.

There's something else: Non-constipating Camalox, with its balanced formulation made by a special process*, is smooth, non-gritty. These qualities, together with its refreshing vanilla-mint flavor, make it easy to take. The first time. Or the hundredth.

And considering that many patients have to spend weeks, months—even years—on antacid therapy, this is no small consideration.

Next time you've got a patient with hyperacidity, prescribe Camalox.

It's the pleasant answer... to an unpleasant condition.

Composition: Balanced formulation of magnesium and aluminum hydroxides with calcium carbonate.

Indications: As an antacid in the treatment and management of peptic ulcer, gastritis, gastric hyperacidity, hiatal hernia, peptic esophagitis, heartburn, indigestion, and upset stomach.

Warning: Camalox should not be used in patients who are severely debilitated or suffering from kidney failure.

Supplied: Camalox Tablets—bottles of 50 tablets and boxes of 100 tablets (in foil strips). Camalox Suspension—white liquid in convenient 12 fluid ounce plastic bottles and economical 16 ounce (pint) bottles.

*Patent pending

CamaloxTM

magnesium and aluminum hydroxides with calcium carbonate

WILLIAM H. RORER, INC.
Fort Washington, Pa. 19034



We're not against all her E. coli...

only the E. coli in her
urinary tract



Macrochantin (nitrofurantoin macrocrystals) is exceptionally effective against E. coli. But it confines its antibacterial action to the urinary tract. It is indicated for the treatment of cystitis,* pyelitis* and pyelonephritis*...nothing else.

Macrochantin is not indicated for therapy of any systemic infection. *And it does not suppress normal bac-*

**Basic in cystitis*, pyelitis*,
pyelonephritis***

The one-tract action of

Macrochantin® Capsules
(nitrofurantoin macrocrystals) 50mg/100mg

Indications: Macrochantin (nitrofurantoin macrocrystals) is indicated for the treatment of pyelonephritis, pyelitis and cystitis due to E. coli, enterococci, Staph. aureus or a small percentage of strains of Pseudomonas, when demonstrated to be susceptible by in vitro susceptibility testing. Also for treatment of such infections when due to some susceptible strains of Klebsiella-Aerobacter and Proteus. It is not indicated for treatment of associated renal cortical or perinephric abscesses, systemic infections or prostatitis, or in any genitourinary tract infections other than pyelonephritis, pyelitis and cystitis.

Contraindications: Anuria, oliguria or extensive impairment of renal function is a contraindication. The drug is contraindicated for infants under one month and in pregnant patients at term. The drug should not be administered to persons who have shown hypersensitivity to nitrofurantoin.

Warnings: Macrochantin may cause hemolytic anemia of the primaquine sensitivity type, apparently linked to a glucose-6-phosphate dehydrogenase deficiency. This deficiency is found in 10 per cent of Negroes and in a small percentage of ethnic groups of Mediterranean

and Near-Eastern origin. Such patients should be observed closely while receiving nitrofurantoin. Discontinue the drug at any sign of hemolysis. Hemolysis ceases on withdrawal. Superinfections may occur, most commonly due to Pseudomonas.

Usage in pregnancy: THE SAFETY OF NITROFURANTOIN DURING PREGNANCY AND LACTATION HAS NOT BEEN ESTABLISHED. IT SHOULD NOT BE USED IN WOMEN OF CHILDBEARING POTENTIAL UNLESS THE EXPECTED BENEFITS OUTWEIGH THE POSSIBLE HAZARDS.

Precautions: Peripheral neuropathy may occur. A fatality has been reported. Predisposing conditions such as renal impairment, anemia, diabetes, electrolyte imbalance, vitamin B deficiency and debilitating disease may enhance such occurrence.

Adverse reactions: Nausea, emesis and diarrhea may occur; reduction in dosage may alleviate these symptoms. Sensitization appearing as cutaneous eruptions or pruritus has occurred. Hypersensitivity reactions resulting in nonfatal anaphylaxis, angioedema, pulmonary infiltration with pleural effusion and eosinophilia have been reported. Other possible

reactions are chills, fever, jaundice, asthmatic symptoms and hypotension. Occasionally headache, dizziness, nystagmus, vertigo, drowsiness, malaise and muscular aches have occurred. Transient alopecia has been reported. Leukopenia, including granulocytopenia, has been reported rarely. The blood picture has returned to normal following cessation of therapy. As with other antimicrobial agents, superinfections by resistant organisms may occur. With Macrochantin, however, these are limited to the genitourinary tract because suppression of normal bacterial flora elsewhere in the body does not occur.

Macrochantin works against a majority of urinary tract pathogens, including some strains of Proteus and Klebsiella-Aerobacter; however, only a small percentage of strains of Pseudomonas are susceptible.

*Due to susceptible organisms.

reactions are chills, fever, jaundice, asthmatic symptoms and hypotension. Occasionally headache, dizziness, nystagmus, vertigo, drowsiness, malaise and muscular aches have occurred. Transient alopecia has been reported. Leukopenia, including granulocytopenia, has been reported rarely. The blood picture has returned to normal following cessation of therapy. As with other antimicrobial agents, superinfections by resistant organisms may occur. With Macrochantin, however, these are limited to the genitourinary tract because suppression of normal bacterial flora elsewhere in the body does not occur.

Dosage: Adult: 50 to 100 mg. four times a day.

Supplied: Macrochantin (nitrofurantoin macrocrystals) Capsules of 50 mg. and 100 mg.

EATON PRODUCT CODE—For easy product identification and verification—Macrochantin Capsules 50 mg. (F03), 100 mg. (F04).



Originators and Developers of The Nitrofurans
EATON LABORATORIES
Norwich International
410 Park Avenue, New York, N.Y. 10022

**Cuando comen lo que les gusta
y no lo que deben...**



ayude a cubrir "el déficit" de vitaminas con

Unicap Therapeutic

10 vitaminas combinadas con 7 minerales

Cada tableta contiene:

Vitamina A	1.5 mg.
Vitamina D	10 mcg.
Mononitrato de Tiamina (B-1)	10 mg.
Riboflavina (B-2)	10 mg.
Acido Ascórbico (C) (como ascorbato de sodio)	300 mg.
Niacinamida	100 mg.
Clorhidrato de Piridoxina (B-6)	2 mg.
Pantotenato de Calcio	20 mg.
Cobalamina (B-12) (como concentrado de cobalamina)	20 mg.
Vitamina E	30 Unidades Internacionales
Hierro (a partir de 50 mg. de sulfato ferroso)	10 mg.
Yodo (como yoduro de potasio)	0.15 mg.
Calcio (como carbonato)	50 mg.
Cobre (como sulfato)	1 mg.
Manganeso (como sulfato)	1 mg.
Magnesio (como sulfato)	6 mg.
Potasio (como sulfato)	5 mg.

Posología: Adultos y niños mayores de 6 años - 1 tableta diaria.

Presentación: Frascos de 30 y 90

Upjohn

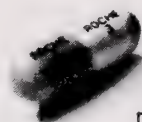
PR 5226 1 MAY, 1969

6811 MARCA REGISTRADA EN E.U.A.: UNICAP THERAPEUTIC

UPJOHN INTER-AMERICAN CORPORATION / CAPARRA / PUERTO NUEVO

How strong must a tranquilizer be for severe anxiety?

As strong as Librium® 25 mg (chlordiazepoxide HCl)



The achievement of desired therapeutic results is often a function of the dosage strength as well as the drug's intrinsic action. Thus, when anxiety is *severe*, the 25-mg strength of Librium frequently provides the necessary antianxiety action with a minimum of unwanted adverse reactions. Librium 25 mg is a convenient dosage form for the relief of severe, incapacitating anxiety, specifically formulated to supplement your counsel and reassurance.

Benefits-to-risks ratio permits higher dosage

For over 13 years, Librium has been recognized for its excellent benefits-to-risks ratio, an asset in the *higher* dosage ranges as in more common clinical applications. Thus, the frequency of dosage with Librium 25 mg can be flexibly adjusted to the needs and response of the individual patient, up to 100 mg daily if required. Total daily dosage for the elderly and debilitated should not exceed 20 mg. When severe anxiety has been reduced, Librium dosage should be correspondingly reduced or discontinued entirely.



basic support
in severe anxiety
Librium® 25 mg
(chlordiazepoxide HCl)
1 capsule t.i.d./q.i.d.



Roche Laboratories
Division of Hoffmann-La Roche Inc
Nutley, N.J. 07110

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Relief of anxiety and tension occurring alone or accompanying various disease states.

Contraindications: Patients with known hypersensitivity to the drug.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation, or in women of childbearing age requires that its potential benefits be weighed against its possible hazards.

Precautions: In the elderly and debilitated and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxious states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also countered are isolated instances of skin eruptive edema, minor menstrual irregularities, nausea, constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, requiring periodic blood counts and liver function tests advisable during protracted therapy.

Supplied: Librium® Capsules containing 5 mg, 10 mg or 25 mg chlordiazepoxide HCl. Libritabs® Tablets containing 5 mg, 10 mg or 25 mg chlordiazepoxide.

~~DISPLAY~~
SHELVES

Julio 1973
Vol. 65, No. 7

THE FRANCIS A. COUNTRYMAN
LIBRARY OF MEDICINE
BOSTON

13 SEP 1973





Everybody experiences psychic tension.



Most people can handle this tension.



Some people develop excessive psychic tension and need your counseling,



and a few may need counseling
and the psychotropic action of Valium® (diazepam).

Before deciding to make Valium (diazepam) part of your treatment plan, check on whether or not the patient is presently taking drugs and, if so, what his response has been. Along with the medical and social history, this information can help you determine initial dosage, the possibility of side effects and the ultimate prospects of success or failure.

While Valium can be a most helpful adjunct to your counseling, it should be prescribed only as long as excessive psychic tension persists and should be discontinued when you decide it has accomplished its therapeutic task. In general, when dosage guidelines are followed, Valium is well tolerated (see Dosage). For convenience it is available in 2-mg, 5-mg and 10-mg tablets.

Drowsiness, fatigue and ataxia have been the most commonly reported side effects.

Until response is determined, patients receiving Valium should be cautioned against engaging in hazardous occupations requiring complete mental alertness, such as driving or operating machinery.



Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, N.J. 07110

Valium® (diazepam)

To help you manage excessive psychic tension

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anti-convulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

Dosage: Individualize for maximum beneficial effect.

Adults: Tension, anxiety and psychoneurotic states, 2 to 10 mg b.i.d. to q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed; adjunctively in skeletal muscle spasm, 2 to 10 mg t.i.d. or q.i.d.; adjunctively in convulsive disorders, 2 to 10 mg b.i.d. to q.i.d. *Geriatric or debilitated patients:* 2 to 2½ mg, 1 or 2 times daily initially, increasing as needed and tolerated. (See Precautions.) **Children:** 1 to 2½ mg t.i.d. or q.i.d. initially, increasing as needed and tolerated (not for use under 6 months).

Supplied: Valium® (diazepam) Tablets, 2 mg, 5 mg and 10 mg; bottles of 100 and 500. All strengths also available in Tel-E-Dose® packages of 1000.

the bare facts.

in many dermatoses* the less they wear,
the more they need...

Vioform[®]-Hydrocortisone (iodochlorhydroxyquin and hydrocortisone)

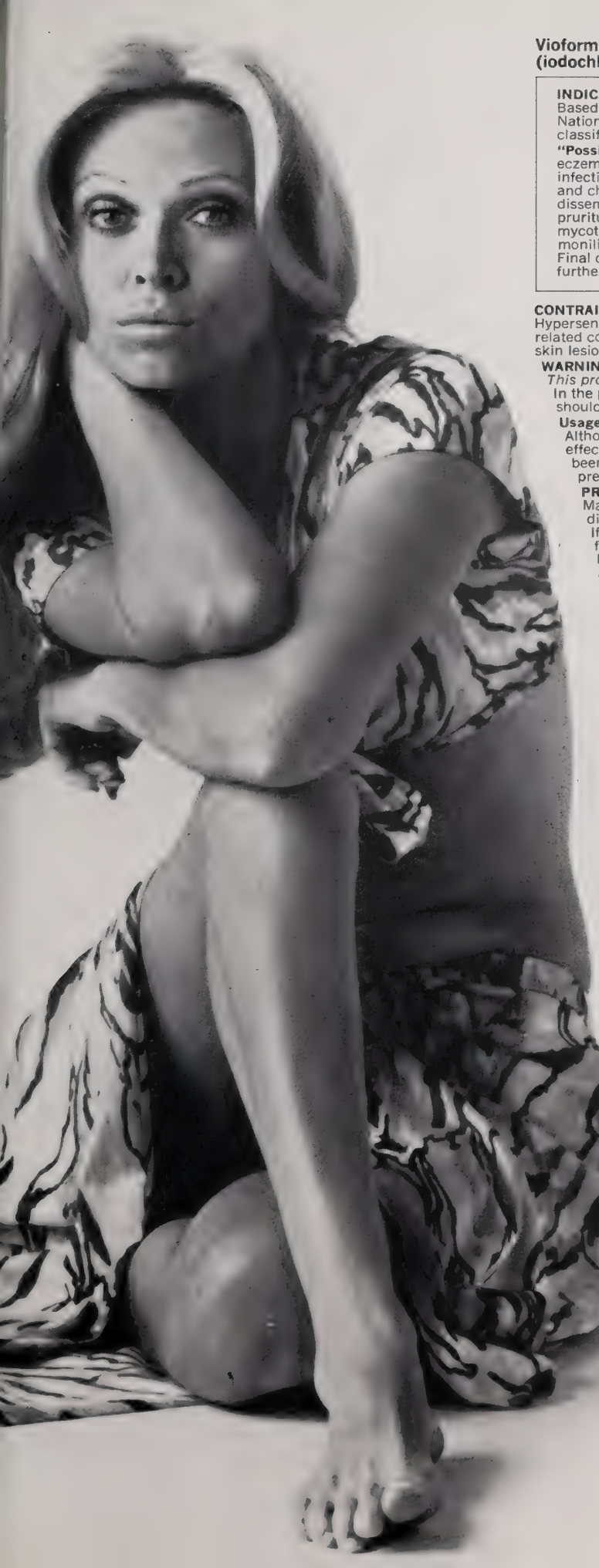
antifungal • antibacterial • anti-inflammatory • antipruritic

Some styles don't leave much to the imagination. And don't provide much cover for common dermatoses, either. Just like plain topical steroids. If the lesion has become infected with fungi or bacteria, plain topical steroids are ordinarily not recommended as sole therapy. Vioform-Hydrocortisone, on the other hand, provides the kind of comprehensive therapy these dermatoses may require. It not only supplies the anti-inflammatory and antipruritic actions of hydrocortisone...but also adds the antibacterial and antifungal actions of Vioform.

*This drug has been evaluated as possibly effective for these indications. See brief prescribing information.

**Another fact...
the most widely
prescribed form...
20 Gm cream**





Vioform®-Hydrocortisone
(iodochlorhydroxyquin and hydrocortisone)

INDICATIONS

Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, FDA has classified the indications as follows:

"Possibly" effective: Contact or atopic dermatitis; impetiginized eczema; nummular eczema; infantile eczema; endogenous chronic infectious dermatitis; stasis dermatitis; pyoderma; nuchal eczema and chronic eczematoid otitis externa; acne urticata; localized or disseminated neurodermatitis; lichen simplex chronicus; anogenital pruritus (vulvae, scroti, ani); folliculitis; bacterial dermatoses; mycotic dermatoses such as tinea (capitis, cruris, corporis, pedis); moniliasis; intertrigo.

Final classification of the less-than-effective indications requires further investigation.

CONTRAINDICATIONS

Hypersensitivity to Vioform-Hydrocortisone, or any of its ingredients or related compounds; lesions of the eye; tuberculosis of the skin; most viral skin lesions (including herpes simplex, vaccinia, and varicella).

WARNINGS

This product is not for ophthalmic use.

In the presence of systemic infections, appropriate systemic antibiotics should be used.

Usage in Pregnancy

Although topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use in pregnant females has not been established. Therefore, they should not be used extensively on pregnant patients in large amounts or for prolonged periods of time.

PRECAUTIONS

May prove irritating to sensitized skin in rare cases. If this occurs, discontinue therapy. May stain.

If used under occlusive dressings or for a prolonged period, watch for signs of pituitary-adrenal axis suppression.

May interfere with thyroid function tests. Wait at least one month after discontinuance of therapy before performing these tests. The ferric chloride test for phenylketonuria (PKU) can yield a false-positive result if Vioform is present in the diaper or urine.

Prolonged use may result in overgrowth of nonsusceptible organisms requiring appropriate therapy.

ADVERSE REACTIONS

Few reports include: Hypersensitivity, local burning, irritation, pruritus. Discontinue if untoward reaction occurs. Rarely, topical corticosteroids may cause striae at site of application when used for long periods in intertriginous areas.

DOSAGE

Apply a thin layer to affected areas 3 or 4 times daily.

HOW SUPPLIED

Cream, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearyl alcohol, spermaceti, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of 5 and 20 Gm. *Ointment*, 3% iodochlorhydroxyquin and 1% hydrocortisone in a petrolatum base; tubes of 5 and 20 Gm. *Lotion*, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearic acid, cetyl alcohol, lanolin, propylene glycol, sorbitan trioleate, polysorbate 60, triethanolamine, methylparaben, propylparaben, and perfume. *Mild Cream*, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a water-washable base containing stearyl alcohol, spermaceti, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of ½ and 1 ounce. *Mild Ointment*, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a petrolatum base; tubes of ½ and 1 ounce.

Consult complete product literature before prescribing.

CIBA Pharmaceutical Company
Division of CIBA-GEIGY Corporation
Summit, New Jersey 07901

2/4766 17

C I B A

BOLETIN

ASOCIACION MEDICA DE PUERTO RICO



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CUBIERTA DEL MES DE JULIO: HOMENAJE AL JIBARO
PUERTORRIQUEÑO



The diabetic
who has
too much...

too much sugar,
too much fat.

Maybe the last thing she needs is more of her own insulin. Especially when you consider that many overweight diabetics already have normal or high levels of endogenous insulin and that insulin is lipogenic.

If she just won't diet and oral therapy is indicated in adult-onset, nonketotic diabetes.

DBI-TD[®] Geigy
phenformin HCl

lowers blood sugar without raising blood insulin.

For complete details, including dosage, please read the prescribing information. It's summarized below.

DBI[®] phenformin HCl
Tablets of 25 mg.
DBI-TD[®] phenformin HCl
Timed-Disintegration
Capsules of 50 and 100 mg.

Indications: Stable adult diabetes mellitus; sulfonyleurea failures, primary and secondary; adjunct to insulin therapy of unstable diabetes mellitus.

Contraindications: Diabetes mellitus that can be regulated by diet alone; juvenile diabetes mellitus that is uncomplicated and well regulated on insulin; acute complications of diabetes mellitus (metabolic acidosis, coma, infection, gangrene); during or immediately after surgery where insulin is indispensable; severe hepatic disease; renal disease with uremia; cardiovascular collapse (shock); after disease states associated with hypoxemia.

Warnings: Use during pregnancy is to be avoided.

Precautions: 1. **Starvation Ketosis:** This must be differentiated from "insulin lack" ketosis and is characterized by ketonuria which, in spite of rel-

atively normal blood and urine sugar, may result from excessive phenformin therapy, excessive insulin reduction, or insufficient carbohydrate intake. Adjust insulin dosage, lower phenformin dosage, or supply carbohydrates to alleviate this state. **Do not give insulin without first checking blood and urine sugar.**

2. **Lactic Acidosis:** This drug is not recommended in the presence of azotemia or in any clinical situation that predisposes to sustained hypotension that could lead to lactic acidosis. To differentiate lactic acidosis from ketoacidosis, periodic determinations of ketones in the blood and urine should be made in diabetics previously stabilized on phenformin, or phenformin and insulin, who have become unstable. If electrolyte imbalance is suspected, periodic determinations should also be made of electrolytes, pH, and the lactate-pyruvate ratio. The drug should be withdrawn and insulin, when required, and other corrective measures instituted immediately upon the appearance of any metabolic acidosis.

3. **Hypoglycemia:** Although hypoglycemic reactions are rare when phenformin is used alone, every precaution should be observed during the dosage adjustment period particularly when insulin or a sulfonylurea has been given in combination with phenformin.

Adverse Reactions: Principally gastrointestinal; unpleasant metallic taste, continuing to anorexia, nausea and, less frequently, vomiting and diarrhea. Reduce dosage at first sign of these symptoms. In case of vomiting, the drug should be immediately withdrawn. Although rare, urticaria has been reported, as have gastrointestinal symptoms such as anorexia, nausea and vomiting following excessive alcohol intake.

(B) 98-146-103-E (6/72)

For complete details, including dosage, please see full prescribing information.

GEIGY Pharmaceuticals
Division of CIBA-GEIGY Corporation
Ardsley, New York 10502

What should a medication for sleep be expected to provide?



Before prescribing Dalmane (flurazepam HCl), please consult Complete Product Information, a summary of which follows:

Indications: Effective in all types of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings and/or early morning awakening; in patients with recurring insomnia or poor sleeping habits; and in acute or chronic medical situations requiring restful sleep. Since insomnia is often transient and intermittent, prolonged administration is generally not necessary or

recommended.

Contraindications: Known hypersensitivity to flurazepam HCl.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. Caution against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Use in women who are or may become pregnant only when potential benefits have been weighed against possible hazards. Not recommended for use in persons under 15 years

of age. Though physical and psychological dependence have not been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage.

Precautions: In elderly and debilitated, initial dosage should be limited to 15 mg to preclude oversedation, dizziness and/or ataxia. If combined with other drugs having hypnotic or CNS-depressant effects, consider potential additive effects. Employ usual precautions in patients who are severely depressed, or with

Sleep for 7 to 8 hours without need to repeat dosage during the night

No sleep medication has been as rigorously evaluated in the sleep research laboratory as Dalmane. Insomnia patients given one 30-mg capsule of Dalmane at bedtime, on average: fell asleep within 17 minutes, had fewer nighttime awakenings, spent less time awake after sleep onset, and slept for 7 to 8 hours with no need to repeat dosage during the night.

Sleep with consistency

Dalmane has been shown to be consistently effective even during consecutive nights of administration. Thus there is little likelihood for the need to increase dosage to maintain therapeutic effect.

Dalmane (flurazepam HCl) is a distinctive sleep medication—a benzo-diazepine specifically indicated for insomnia. It is not a barbiturate or methaqualone, nor is it related chemically to any other available hypnotic.

Sleep with relative safety

Chronic tolerance studies have confirmed the relative safety of Dalmane; no depression of cardiac or respiratory function was noted in patients administered recommended or higher doses for as long as 90 consecutive nights. Dalmane is generally well tolerated and morning "hang-over" is relatively infrequent. Dizziness, drowsiness, lightheadedness and the like have been the side effects noted most frequently, particularly in elderly and debilitated patients. (An initial dose of Dalmane 15 mg should be prescribed for these patients.)

DALMANE®

(flurazepam HCl)

When restful sleep is indicated

One 30-mg capsule h.s.—usual adult dosage
(15 mg may suffice in some patients)

One 15-mg capsule h.s.—initial dosage for elderly or debilitated patients.

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ent depression or suicidal tendencies. periodic blood counts and liver and kidney function tests are advised during repeated therapy. Observe usual precautions in presence of impaired renal or hepatic function.

Adverse Reactions: Dizziness, drowsiness, lightheadedness, staggering, ataxia and falling have occurred, particularly in elderly or debilitated patients. Severe ataxia, lethargy, disorientation and coma, probably indicative of drug intolerance or overdosage, have been reported.

Also reported were headache, heartburn, upset stomach, nausea, vomiting, diarrhea, constipation, GI pain, nervousness, talkativeness, apprehension, irritability, weakness, palpitations, chest pains, body and joint pains and GU complaints. There have also been rare occurrences of sweating, flushes, difficulty in focusing, blurred vision, burning eyes, faintness, hypotension, shortness of breath, pruritus, skin rash, dry mouth, bitter taste, excessive salivation, anorexia, euphoria, depression, slurred speech,

confusion, restlessness, hallucinations, and elevated SGOT, SGPT, total and direct bilirubins and alkaline phosphatase. Paradoxical reactions, e.g., excitement, stimulation and hyperactivity, have also been reported in rare instances.

Dosage: Individualize for maximum beneficial effect. *Adults:* 30 mg usual dosage; 15 mg may suffice in some patients.

Elderly or debilitated patients: 15 mg initially until response is determined.

Supplied: Capsules containing 15 mg or 30 mg flurazepam HCl.

Opinion & Dialogue

"Prescription drugs – who should determine the maker?"

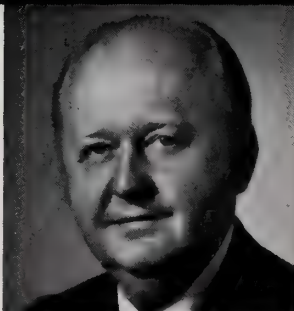
Dispenser of
Medicine

Clifton J. Latiolais
President
American
Pharmaceutical
Association



Maker of
Medicine

C. Joseph Stetler
President
Pharmaceutical
Manufacturers
Association



"Too many doctors are indifferent to the economic consequences of their decisions." So stated a recent issue of *Medical News Report* (December 4, 1972), an independent weekly newsletter published by former AMA Chief Executive F. J. L. Blasingame, M.D.

Doctor, are you indifferent...?

In discussing an anticipated increase in Blue Shield rates, Dr. Blasingame's newsletter had this to say:

"In general, it can be said, MD's have given the impression they are not particularly concerned with the increase in cost of health care to their patients..."

"True, an MD's training is primarily scientific, but in the real world of practice, all of his scientific decisions have a price tag, or an economic impact. The economics of health care beckon the practitioner's attention. Concern for economics of medicine

When the pharmacist recommends that a drug product other than the one ordered be dispensed, the prescriber invariably permits the change when he feels the best interests of the patient will be served.

Shortcomings of Pro-Substitution Argument

The fact remains that it is necessary for the prescriber to know that the change is being contemplated, and to be in a position to consent or demur. Without that opportunity, the unilateral decision of the pharmacist, made in the absence of clinical knowledge of the patient, could expose him to needless risks, and in addition, jeopardize the relationship between the professions of Pharmacy and Medicine. In my view, there is nothing in the pro-substitution argument that offsets these risks.

The Issue of Drug Knowledge

Substitution advocates claim that the primary justification for changing the rules is the desire to better utilize pharmacists' knowledge about drugs. Yet the pharmacist's task to keep current on the entire field of drug therapy, to some degree, puts him at a disadvantage. Most often, a practicing physician will need expert knowledge of no more than 25

CORONARY ARTERIOGRAPHY - A REVIEW (FIRST PART)

Charles D. Johnson, MD, FACP, FACC

The Problem

Coronary artery disease (CAD) due to coronary atherosclerosis, the Black Death of the 20th century, the major cause of death in North America and the Western World, causes some 625,000 deaths annually in the United States (US) and is also becoming a major scourge and cause of death in Puerto Rico (1, 2). Every year about a million persons in the US experience either a myocardial infarction (MI) or sudden coronary heart disease (CHD) death (1). More than one-half of the deaths in the US are due to diseases of the heart and blood vessels, the majority being secondary to CAD. It has been estimated that about 5 percent of the population has definite or suspect CHD. A North American male has about one chance in five of developing clinical CHD before age 60 years, mostly in the form of MI (1). Middle-aged persons who survive their first attack are five times as likely to die within five years as those without a history of previous coronary disease, usually from recurrent acute coronary episodes (1). The average survival after the onset of angina pectoris (AP) is 4 years, and the average 5 year mortality ranges from 30-40 percent (3). More recent studies suggest that the annual mortality is only about 4 percent. CAD is often present in asymptomatic subjects.

Some 25-30 percent of patients with incident cases of MI die suddenly. In about two-thirds of all deaths due to arteriosclerotic heart disease (ASHD) the individuals die outside of a hospital or are dead on arrival to the hospital. Twenty-three percent of individuals with ASHD had seen a physician within a week before death (4, 5). Sudden death (SD) as the first apparent manifestation of the disease, may vary from 20-25 percent (6).

Physicians who were formerly expert in and occupied with diseases of tropical medicine, now find themselves confronted with this new worldwide plague of mankind, coronary atherosclerosis, its manifestations of AP, MI, SD and other complications. This is presently being actively pursued here in Puerto Rico (7).

The history, physical examination, the electrocardiogram (ECG) and sometimes, exercise tests, have been the standard means of diagnosing and coping with the manifestations of CHD for decades (8, 9, 10, 11, 12). These methods are of paramount importance and usually they suffice to meet the challenge, but unfortunately, not infrequently are inadequate or misleading, even when performed in the best of faith, with time and the best available interpretations. Patients have been treated and regarded for years as victims of this verdict, bound under long medical regimes, restrictions, and the implications with which a diagnosis of "ASHD" or heart disease carries, when none such exists (13). On the other hand, and to the chagrin of the physician, the 50 years old business executive may die in the parking lot, or within a few weeks, after receiving his "checkup" and a clean bill of health based upon the mentioned modalities and a normal ECG.

Various noninvasive methods have also made remarkable strides in this field in recent years (14, 15).

The number of "under-and over-diagnoses", misdiagnoses and iatrogenic heart disease on the basis of these limitations, an inadequately taken history and ECG interpretation, may approach epidemic proportions.

The Limitations

Some one-half to three-fourths of patients with AP have a normal resting ECG. Extensive diffuse disease of all three major coronary arteries may be present with a normal ECG. Although usually of less magnitude, exercise stress tests may be falsely positive in as high as 39 percent, and falsely negative in up to 57 percent of cases (16). Widespread CAD or even a previous MI may be associated with a negative postexercise ECG.

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Serum enzymes, hypercholesterolemia and other coronary risk factors may not accurately identify the CHD patient in an individual instance (17).

Martínez-Ríos and colleagues found in 480 consecutive coronary arteriograms, 21 cases with normal resting ECG's associated with complete or nearly complete occlusion of one or more of the three major coronary branches. All 21 cases had AP and 6 had clinical evidence of MI six months or before the arteriogram (18). In young men about one-half of the patients with total occlusion of only the right or circumflex coronary artery, and about one-third of those with total occlusion of the anterior descending artery had no electrocardiographic or ventriculographic evidence of infarction (19). The ECG may sometimes be normal despite a long history of severe angina with diffuse coronary narrowing and even with proximal occlusions (20). Arteriosclerosis in one artery may give the same clinical findings, ECG and lipids as involvement of four arteries (21).

There are more than 25 causes of Q waves in the ECG other than the most important cause, CHD: several conditions may produce ST elevation other than injury from coronary atherosclerosis, and there are some 150 or more causes of T wave changes, not attributable to myocardial ischemia from atherosclerosis of the coronary arteries. The best electrocardiographer can aspire to an accuracy rate in MI of about 85 percent; this figure may be less on the basis of autopsy correlation, about 62 percent. The presence of multiple infarctions, subendocardial infarctions, dorsal lesions, the W-P-W syndrome, LBBB, ventricular hypertrophy, digitalis, electrolyte changes and the ECG instrumental characteristics may account for this low diagnostic definition.

Kalbfleisch and associates found disappearance of the electrocardiographic evidence of necrosis in 12 percent of 775 patients with healed infarctions (22). A large Mayo Clinic autopsy series noted that only 50 percent of all healed MI's and 60 percent of acute infarctions established at necropsy had been clinically diagnosed or suspected during life (23).

Marriott quoted Frank Wilson who expressed the disillusioned regret that most people were in greater danger of having their peace and happiness shattered by an erroneous electrocardiographic interpretation than of being injured by an atomic bomb (24). As Leatham stated, the ECG only tells us of the state of the heart muscle which may be quite normal even with advanced disease of the coronary arteries (25). However, one of our very best tests, the ECG, and the arteriogram are rightly

regarded as being complimentary, and the arteriographic findings must be correlated with the clinical manifestations (26, 27).

In one large series of a 1000 patients about 37 percent of patients who had been told by a physician that CAD was present or suspected, had no significant obstruction and some 27 percent had normal coronary arteriograms (28). Some 20-35 percent of patients referred for coronary arteriography (CA) have normal arteriograms. Sones has thus found 1000 patients annually in his laboratory who were misdiagnosed, and estimated a one million dollars productivity savings in his laboratory alone by returning the patients to work. Normal coronary arteriograms were later found in patients following years of well-intended therapy with vasodilators, sedatives and anticoagulants, after addiction to narcotics, and after useless surgery and radioactive iodine therapy (13, 29).

Selective CA has become the most specific diagnostic procedure available to detect coronary atherosclerosis and its complications, and to demonstrate its site and extent, in the living patient. The procedure may be performed either by the Sones method via a brachial arteriotomy (13, 30) or by the Judkins method via a femoral percutaneous approach, employing pre-formed catheters (31, 32, 33).

Thus, within this background of limitations of previously employed methods of diagnosis, the indications for selective CA may be discussed. These indications represent those presently generally accepted, and have been emphasized by many outstanding physicians (3, 13, 25, 30, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54).

Indications (Table I)

1. Any patient with the frequent dilemma of CAD being suspected, but which cannot be either documented or excluded. A yes or no answer is valuable in management. The procedure should be performed as soon as possible after the appearance of symptoms and 4-6 weeks after an acute MI, and before major modifications in the patient's life are advised.

2. The evaluation of chest pain, particularly pain of atypical nature and uncertain origin and associated with nondiagnostic or atypical features, and nondiagnostic history, physical findings, ECG, exercise stress tests, serum enzymes and other laboratory data (UGI, gall bladder x-rays, etc.); the resting and exercise ECG may be normal or nonspecific. Esophagitis, pericarditis,

TABLE I: CONSIDERATIONS AND INDICATIONS FOR CORONARY ARTERIOGRAPHY *

Evaluation of the patient with:

Chest Pain, especially when atypical
Angina Pectoris
Myocardial Infarction, or suspicion of infarction.

To diagnose or to exclude the diagnosis of coronary artery disease.

Evaluation of the young person with angina pectoris or myocardial infarction.

Evaluation of the patient with:

Obscure heart disease
Cardiomyopathy
Unexplained congestive heart failure
Unexplained arrhythmias or electrocardiographic abnormalities, Q waves, BBB, etc., especially of recent onset; coronary mimics
Coronary artery anomalies.

Determination of work status; Insurance; Life modes, etc.

Military, or aerospace medical decisions.

Psychological reasons. Reassurance. To clarify, verify or exclude the diagnosis.

Evaluation of LV hemodynamics.

Research purposes—drug effects; physiology; correlation with exercise stress tests, the ECG.
Natural history of coronary atherosclerosis.

Evaluation of the patient with valvular heart disease (especially aortic valve disease) and chest pain—
Pre surgery.

For therapy and management of the patient with coronary artery disease — medical, diet, exercise, surgical.
Rehabilitation.

For selection of patients for myocardial revascularization surgery; type of procedure; development of surgical techniques.
Pre-infarctional angina
Acute myocardial infarction, with shock, severe failure.
Ventricular aneurysm, dyskinesis—with failure.

Evaluation of post-operative myocardial revascularization status.

For prognostic implications.

* See text for details.

hiatus hernia, cervical arthritis, chest wall pain, gall bladder disease, psychoneurosis and lung disease are differential diagnostic problems.

3. Atypical AP in respect to: location of pain, precipitating factors, sites of radiation, quality, duration, factors that bring relief and the course; AP not relieved by rest or rapidly by nitroglycerine (NG) or relieved only after one-half hour or more; typical

AP except for lack of relief with NG and a negative exercise test (double Master's test, submaximal exercise); atypical AP with a positive exercise test (42). A positive exercise stress test without a history of pain may be an indication for the study in certain good laboratories.

4. In most patients with AP and/or MI, especially if they are less than 50-60 years of age, in order to

plan future therapy-medical or surgical (Some would recommend it in all patients with AP) — Diet, rehabilitation, exercise program, vasodilators, antilipid agents, propranolol, anticoagulants, vein bypass grafts, etc. (55). Some patients may be candidates for prophylactic surgery. It is important to know the extent of disease and collaterals. Intractable AP with or without a history of MI. Chronic ischemic heart disease with or without a history of MI, in the absence of cardiomegaly and congestive heart failure. In stable AP in patients 50 years or less of age who still have limiting symptoms after 3-6 months of medical therapy. In patients with a previous history of MI, and persistent AP (these patients generally have stenosis or occlusion of at least one major coronary artery). In the patient with a history of MI, but who is now asymptomatic.

5. Patients in whom the diagnosis of a MI is suspect, but in whom the features, history, physical findings, ECG and laboratory data are atypical or nondiagnostic.

6. The young patient with AP, or premature MI or recurrent infarctions (even if asymptomatic) with precocious atherosclerosis and hypercholesterolemia, with or without other risk factors of hypertension, diabetes mellitus, obesity, absent ovaries, etc.; young females with MI's who are taking oral contraceptives (56). However, it may be of limited value in the study of individuals with risk factors (49). Recent onset of AP in a young person.

7. Patients with obscure or ill-defined heart disease, such as unexplained cardiomegaly or unexplained progressive congestive heart failure. CHD may occasionally manifest in this fashion. To exclude serious silent disease. Right ventricular hypertrophy with AP.

Patients with the several types of cardiomyopathies, or when a cardiomyopathy is suspected. One study found characteristic coronary arteriographic patterns in patients with obscure cardiomyopathies (57), although the major coronary arteries are generally believed to be normal. A cardiomyopathy and CHD may mimic each other, or both conditions may be present in the same patient. Angina pectoris may be a symptom of Idiopathic Hypertrophic Subaortic Stenosis (IHSS), and IHSS may present in the elderly patient also. CAD patients may present as a congestive cardiomyopathy — "Ischemic Cardiomyopathy" (58). Infarction patterns may be seen in cardiomyopathies and thus be misleading (59, 60). Gulotta and associates found 10 patients within a 2-year period with this combination of diseases; all had been referred with the diagnosis of AP due to CAD; also Rheumatic Heart Disease (RHD) with valvular AS and papillary muscle dysfunction had been considered. So they recommend that CA be done in patients

over 30 years of age with presumed IHSS and AP; and that patients with suspected CAD but with atypical angina, obscure or changing murmurs, unusual response to therapy, brisk peripheral pulses, or suggestive arterial pressure tracings, should be checked for coexisting IHSS. This is especially important if coronary artery surgery is contemplated, or if NG is administered (60). An evaluation of ventricular size and function should also be made.

Patients in whom a differential diagnosis of restrictive cardiomyopathy and chronic constrictive pericarditis without calcification presents a problem (61).

8. To aid in diagnosis and surgical management of myocardial tumors. Patients with syphilis and chest pain, to evaluate for coronary ostial stenosis. To evaluate patients with chronic heart block; or with aortic aneurysmal or occlusive disease (Barlow's syndrome).

9. Patients with coronary artery anomalies—AV fistulas, coronary arteriocameral fistulas, aneurysms (62), Bland-White-Garland syndrome. Anomalous origin and course of the coronary arteries in congenital heart disease—Tetralogy of Fallot, pseudotruncus, the different types of transpositions of the great arteries. Children or young adults with MI's.

10. Patients with unexplained arrhythmias, recurrent VT, conduction defects, ST segment and T wave abnormalities; Lone atrial fibrillation; and premature ventricular beats — recent studies found a 6-10 times increased incidence of SD in such patients (44). LBBB may mask an infarction; although LBBB is usually due to organic heart disease, it may run a benign course. The sudden appearance of RBBB in the adult causes concern.

11. Patients with certain electrocardiographic findings not easily explained, especially abnormal Q waves, and particularly when the patient has chest pain. Wide Q waves may be due to positional factors, atrial and ventricular hypertrophy, myocardial infiltrative diseases, cardiomyopathies, acute pulmonary embolism and other less commonly considered entities. A W-P-W pattern with broad Q waves continues to be mistakenly diagnosed as a MI, as does the pseudo-anterior and pseudo-diaphragmatic patterns of pulmonary emphysema and cor pulmonale (63). Certain congenital conditions may show abnormally located Q waves, QS or QR complexes — corrected transposition of the great vessels, Ebstein's Anomaly. These diseases can usually be diagnosed by conventional means.

12. The patient with chest pain or other suspicious manifestation of CHD in whom the physician is unable or unwilling to take a stand, and thus inform his patient whether he or she does or does not have CHD (36). A

frequent pattern seems to be the young or middle-aged, obese neurotic female or anxious male who frequents the hospital emergency ward with atypical chest pain and nonspecific ST segment and T wave abnormalities. Patients who have received conflicting opinions and recommendations due to physician differences in diagnosis and interpretation (42).

13. To allay the fears and doubts of patients and their physicians, that the patient's chest pain is benign (3), and to reassure patients who are despondent, fearful and anxious over the mistaken diagnosis of CHD, and the armamentarium of drugs prescribed for such—psychological implications. To deal with emotional patients who have experienced frequent doctor contacts, and fears generated by well-meaning physicians. Fear of SD. Fear in the situation of a positive family history of CAD, and lipid abnormalities.

14. In patients where job opportunities, occupation, retirement, work capabilities, social security, life insurance, marriage and future plans are at stake. Dangerous jobs, such as public drivers and pilots.

15. In patients in military and aerospace medicine; it may be of value in administrative decisions as to fitness for return to active duty, flying status, retirement or assignment to isolated areas or combat zones; compensation, future careers, before discharge from the Service. It is important in aircrew where there is the slightest question of CAD; to evaluate ST and T changes, typical and atypical chest pain, silent and overt MI's, cardiomegaly, peripheral arteriosclerosis and LBBB (64, 65). Gracey and associates studied 5 patients with LBBB and normal arteriograms. They also discovered the mistaken diagnosis of "ASHD" in patients already discharged from the Navy and receiving disability compensation—who demonstrated normal arteriograms (66).

16. In patients with CHD for research and study purposes (38). Natural history of coronary atherosclerosis (67). Progression of mild to moderate CAD in initially nonsurgical patients, when functional status is stable or deteriorates (34). Study of drug effects on the coronary circulation. Study of the development of collateral circulation, types of arterial patterns. Correlation of anatomy and function, with symptoms and patterns of presentation of CHD. Prognosis.

17. In patients who merit CA, left ventricular (LV) angiography is routinely performed to evaluate LV contractility, areas of asynergy, aneurysms, presence of mitral regurgitation, as the status of the muscle is a prime factor in operability and decisions on type of drug or exercise therapy. Other hemodynamic and metabolic measurements may be obtained at the same

catheterization—LV end-diastolic pressure and cardiac output, ventricular volume, ejection fraction, coronary blood flow, AV oxygen difference, lactate status, atrial pacing (44, 68), and rise in the LV end-diastolic pressure after angiography (69).

18. Patients with anginal-type chest pain, syncope and aortic valve disease, and in the older (or any) patient with aortic valve or mitral valve disease, in whom surgery is being considered (open heart operations in patients suspected or known to have CHD); mitral regurgitation of unknown etiology. The presence of significant coronary atherosclerosis may affect the operability, risks, benefits and long-term prognosis of aortic and mitral valve replacement, and in itself may require concomitant coronary artery revascularization surgery, and explain the chest pain or contribute to it. Some surgeons use coronary ostial cannulation and perfusion. Seven to 21 percent of patients with valvular heart disease have CAD; however, AP may be due to aortic valve disease in the absence of CAD (70, 71, 72). Although it has been recommended that CA be performed routinely in patients (especially over 40 years of age) undergoing valve replacement, a recent study found that it may be omitted in many patients who have no symptoms of ischemic heart disease (angina), and who lack risk factors known to increase its incidence (73).

19. In patients in whom myocardial revascularization surgery is indicated. The specific indications for this are presently controversial, but may comprise the following: severe, disabling and intolerable pain (AP) despite an adequate period of optimal medical care; progressive worsening of the disease process; prevention of recurrent MI, especially in younger patients (< 60 years) who may have had extensive and repeated MI's; post-infarction angina; acute MI; prevention of infarction in the prodromal period; myocardial salvage in patients who develop MI while awaiting bypass graft; life salvage in patients with uncontrollable ventricular arrhythmias, heart failure or shock; severe segmental stenosis (70 percent) or completely occluded proximal coronary arteries with good distal runoff (obstruction < 50 percent and circumference > 4mm) that is visualized directly or indirectly by collateral circulation; functional myocardium in the area of prospective revascularization; high-grade stenosis of the main left coronary trunk. Demonstrable patent distal segments, although desired, are said not to be absolutely required, as surgical exploration or gas endarterectomy may reveal or establish a graftable "runoff" channel. Indirect implantation surgery may be applied even in patients

with severe and diffuse disease, and with minimal LV fibrosis (9, 74, 75, 76, 77, 78). Selected patients with mild chronic LV failure may possibly be operable (79).

Cardiac revascularization surgery consists of different types of surgical procedures — patch graft (rare), endarterectomy (gas, conventional), internal mammary artery implants (infrequently done as the only procedure), mammary artery-to-coronary artery bypass (80, 81), venous graft bypassing occluded segment and most popularly at the present time, the saphenous vein aortic-coronary artery bypass graft. Resection of areas of dyskinesia or LV aneurysms require coronary and ventricular angiography (size, thickness of wall of aneurysm, LV failure). The coronary arteriogram is absolutely necessary to identify the presence, extent and location of the obstructive lesions and the size and presence of good distal vessels and runoff (75, 77, 78).

As an emergency procedure in patients with Pre-Infarctional Angina or Impending MI, or acute MI in intractable cardiogenic shock (after stabilization with assisted circulation), with ventricular failure or persistent pain, if immediate vein bypass surgery is contemplated (34, 77, 78, 82, 83, 84).

20. To evaluate the results of cardiac revascularization surgery—status and patency of vein grafts and implants, re-evaluation of the patient's arterial system for any progression of the basic disease and flow patterns, and postoperative hemodynamic studies—characteristic electrocardiographic changes following injection, blush, venous filling, etc. This objective information is absolutely necessary, and may be obtained in the early post-operative period and repeated months and years later (85, 86, 87, 88).

21. CA performed in the operating room (OR) may be valuable for the immediate evaluation of bypass grafts (distal anastomosis, distal runoff) before closure of chest, for impending or acute MI, and research. The seriously ill patient could be transferred directly to the OR. The procedure adds < 10 minutes to the total operating time (89). One of the equipment manufacturers has just marketed a mobile x-ray system designed for the OR.

22. Showing patients their normal coronary arteriograms may be of therapeutic value, a means of reassurance, and, an aid in restoring the patient to employability. If CAD is found, this may foster the patient's motivation to follow therapy more meticulously and prompt him to change dietary and smoking habits (52).

Others would be more conservative in their indications, emphasizing risks and costs of the procedure (45). Patients with AP easily controlled by drugs (as the protective effects of aortic-coronary bypass grafts have not been proven), patients presenting for the first time with AP, especially if they fall in the low risk group—normal ECG and blood pressure—(prognosis for life is only slightly less good than that of the normal population) (37), patients with mild typical AP, and patients who have recovered from their first uncomplicated acute MI, especially in the absence of preceding anginal pains, would not be submitted to CA; neither would all patients of "coronary age" who require cardiac operations. Asymptomatic "ischemic" changes present on the ECG or during treadmill testing would not be a sufficient indication (51). Although its use to evaluate asymptomatic men older than 40 years has been mentioned, it is not indicated for mass screening of the general population (49). Baltaxe and Levin divided their indications for CA into two categories, 1) unquestionable, and 2) debatable (47).

The indications for CA in the final analysis, depend much upon the physician's belief in, or the indications for, coronary surgery in a given institution. In some centers all patients with AP have surgery, and thus require arteriography, while in others surgery is offered only to those patients who are severely symptomatic and have not responded to medical therapy (37, 48).

Contraindications

Exact contraindications for CA are still controversial, but may comprise the elderly patient with MI, associated with other diseases, the grossly obese—until weight reduction is attained (excessive scatter radiation and equipment damage may occur in patients > 40 lbs. overweight), significant cardiomegaly due to diffuse scar tissue replacement fibrosis following multiple previous MI's, the presence of hypokalemia, recent significant electrocardiographic changes, the patient with an established acute MI if the symptoms are of longer than 6 hours duration, and the presence of LV failure, shock, impending MI or acute MI, unless immediate surgery is contemplated. The absence of adequate diagnostic and radiological equipment and the unavailability of trained personnel and physicians for the performance and interpretation of the studies are of course contraindications. The absence of a complete surgical team would dictate restraint (34, 37, 47, 48, 50, 51). This study, perhaps more than any other, requires perfec-

tion in all phases, or else it is probably best left undone. The occasional coronary arteriographer, as is the occasional cardiac surgeon, is vigorously discouraged (90, 91).

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EFFECTO NEFROTOXICO DE LOS AGENTES ANTIMICROBIANOS

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La administración de agentes antimicrobianos a pacientes con insuficiencia renal ha ido diseminándose y aumentando a medida que las modalidades terapéuticas modernas del síndrome urémico se hacen más accesibles a un mayor número de pacientes y su vida es prolongada exitosamente.

Como casi todos los agentes antimicrobianos poseen una toxicidad inherente hacia el organismo humano y en su gran mayoría son excretados por la vía renal, es necesario modificar la dosificación de estos agentes cuando se administran a pacientes con insuficiencia renal.

La acumulación en sangre de los preparados antimicrobianos aumenta a medida que la función renal disminuye. Cuando la función renal cae por debajo del 30 por ciento de lo normal, el riesgo de acumulación a niveles tóxicos es mucho mayor, pudiendo ésta afectar el riñón, el hígado, la médula ósea, el sistema nervioso central y el octavo nervio cranial, tanto en su porción colinear como vestibular. El daño puede ser severo o leve, permanente o temporero. En la mayor parte de los casos el grado de afectación correlaciona con los niveles del agente en sangre. Por esta razón, se hace imperativo modificar la dosificación de agentes antimicrobianos en pacientes azotémicos y urémicos.

Factores que Afectan la Dosificación

En términos generales, no es necesario modificar la dosificación de antimicrobianos mientras la función renal se mantiene sobre el 30 por ciento del valor normal. Una vez que cae por debajo del 30 por ciento, la retención de los antimicrobianos en sangre hace imperativo ajustar la dosis y la frecuencia de administración. Cada agente presenta características individuales de acuerdo a su toxicidad inherente, metabolismo en el

organismo y su modo de excreción. El uso de cada antimicrobiano en presencia de azotemia tiene que individualizarse, ya que las restricciones de uno no aplican necesariamente a otros.

Debe evaluarse la función renal antes, durante y al finalizar el curso de tratamiento en pacientes azotémicos o urémicos. Su dosificación debe modificarse aun más si la función renal cae durante la administración del agente antimicrobiano.

En el fallo renal agudo el curso rápido de la condición produce cambios súbitos en función renal de día a día. En estos casos la modificación de la dosis debe ser más cuidadosa y frecuente o de lo contrario el control de los niveles en sangre sería errático.

Debe usarse la vía parenteral para la administración de antimicrobianos en presencia de azotemia, ya que la absorción de las drogas por el tracto gastrointestinal puede ser errática. El inducir diuresis con diuréticos potentes en pacientes con insuficiencia renal es parte importante de su tratamiento, sin embargo una diuresis vigorosa puede aumentar la concentración sérica de agentes antimicrobianos pudiendo estos alcanzar niveles tóxicos por hemoconcentración.

Como prueba de función renal para la evaluación y seguimiento de estos casos, recomendamos la depuración de creatinina endógena de 24 horas corregida a 1.73m^2 de superficie corporal. Su valor normal es de $130\text{ cc/min}/1.73\text{m}^2$. Sin embargo para propósitos de modificación en dosis de antimicrobianos consideramos $70\text{ cc/min}/1.73\text{m}^2$ o más como normal.

Agentes Antimicrobianos Individuales

1. Tetraciclinas

Todas las tetraciclinas son capaces de inducir azotemia pre-renal debido a su efecto anti-anabólico. Su administración puede inducir disturbios gastrointestinales severos, aumento en la azotemia, hiperfosfatemia y acidosis en pacientes con insuficiencia renal. En general, este grupo de drogas debe evitarse en lo posible en presencia de azotemia.

TABLA I: DOSIFICACION DE ANTIMICROBIANOS EN INSUFICIENCIA RENAL

Agente Antimicrobiano	Por ciento de Función Renal (C_{cr})	
	10 - 30 Por ciento	< 10 Por ciento
Tetracilinas	No se recomienda su uso	
Cloramfenicol	No requiere ajuste	
Penicilina G	Dosis usuales, evitar dosis altas	
Carbenicilina	2-4 gm cada 6-12 hrs.	2 gm, luego 1 gm cada 8-12 hrs.
Meticilina	1-2 gm cada 3-6 hrs.	1-2 gm cada 4-8 hrs.
Cloxacilina	No requiere ajuste	0.25-0.5 gm cada 6 hrs.
Dicloxacilina	No requiere ajuste	0.25-0.5 gm cada 6 hrs.
Oxacilina	No requiere ajuste	0.25-0.5 gm cada 6 hrs.
Cefalotina	1-2 gm cada 6-8 hrs.	1 gm cada 6-24 hrs.
Cefaloridina	0.5 gm cada 12 hrs.	0.5 gm cada 24 hrs.
Cefalexina	0.5 gm cada 8-12 hrs.	0.5 gm cada 24-48 hrs.
Lincomicina (oral)	0.5 gm cada 8 hrs. por 3 dosis, luego 0.5 gm cada 6-12 hrs.	0.5 gm cada 8 hrs por 3 dosis, luego 0.5 gm cada 6-12 hrs.
Lincomicina (parenteral)	0.6 gm cada 8 hrs. por 3 dosis, luego 0.6 gm cada 12 hrs.	0.6 gm cada 8 hrs. por 3 dosis, luego 0.6 gm cada 12 hrs.
Eritromicina	No requiere ajuste	
Kanamicina (oral)	1 gm cada 8-12 hrs.	(?) 1 gm cada 24 hrs.
Kanamicina (IM)	7.5 mg/kg cada 12 hrs. x 2 dosis, luego 7.5mg/kg cada 1-2 días	7.5 mg/kg cada 12-24 hrs x 2 dosis, luego 7.5 mg/kg cada 3-6 días
Colistimetato	(?) 1.6 mg/kg cada 8 hrs. x 3 dosis, luego 1.3 mg/kg cada 12 hrs.	(?) 1.6 mg/kg cada 12 hrs x 2 dosis, luego 0.8 mg/kg cada 12-18 hrs.
Gentamicina	Ver Texto	Ver Texto
Furadantina	Uso no recomendado	Uso no recomendado
Mandelamina (R)	Uso no recomendado	Uso no recomendado
Acido Nalidíxico	1 gm cada 6 hrs. x 12 dosis, luego 1 gm cada 12 hrs.	Dosificación no determinada
Sulfonamidas	Uso no recomendado	Uso no recomendado

(?) = Dosificación no ha sido determinada con exactitud.

2. Cloramfenicol

En presencia de una función hepática normal, el paciente azotémico inactiva el *cloramfenicol* normalmente. Sus metabolitos no parecen ser tóxicos. Por lo tanto, no es necesario hacer ajustes en la dosificación en presencia de azotemia. No obstante, las precauciones usuales deben observarse cuidadosamente al usar esta

droga en presencia de insuficiencia renal.

3. Las Penicilinas

La *penicilina* no presenta efectos tóxicos cuando se administran en dosis usuales a pacientes azotémicos. Por lo tanto, su dosificación no requiere ajuste. Es bueno recordar que la *Penicilina G* contiene 1.69 mEq de potasio por millón de unidades y esto puede agravar

la hiperkalemia que acompaña el fallo renal severo. En dosis altas estas drogas han producido desórdenes convulsivos, alucinaciones e hiperirritabilidad. Por esta razón, las dosis altas se deben evitar en presencia de insuficiencia renal. La *Carbenicilina* puede inducir una diátesis hemorrágica en presencia de azotemia. La *Meticilina* se excreta principalmente por vía renal y por lo tanto se retiene en presencia de azotemia.

4. *Cefalosporinas*

La *Cefalotina* se excreta mayormente por vía renal y demuestra una toxicidad muy baja. Por el contrario la *Cefaloridina* y *Cefalexina* se excretan más lentamente y sus niveles y mediavida en sangre aumentan en fallo renal.

5. *Lincomicina*

Pacientes con insuficiencia renal retienen *Lincomicina* en sangre y su período de mediavida se prolonga. Esto se debe a que su excreción es mayormente por vía renal.

6. *Eritromicina*

La *Eritromicina* es una droga inocua, no se retiene considerablemente en fallo renal y su uso no requiere ajuste en la dosificación.

7. *Kanamicina*

La *Kanamicina* se excreta en su forma activa por filtración glomerular. La nefrotoxicidad es usualmente reversible, no así su ototoxicidad, la cual es bilateral e irreversible en muchos casos. Sus efectos tóxicos pueden ser minimizados si su dosis es modificada.

8. *Polimixinas*

Las *Polimixinas* interfieren con la conducción nerviosa a nivel de la placa neuromotora y pueden inducir apnea. Es preferible usar el *Colistimetato* en lugar de la *Polimixina B*, ya que es menos nefrotóxico.

9. *Gentamicina*

La *Gentamicina* demuestra muy poca latitud

entre sus niveles terapéuticos y sus niveles tóxicos en sangre. Se excreta principalmente por filtración glomerular y por lo tanto se retiene considerablemente en presencia de azotemia. Produce ototoxicidad y nefrotoxicidad. La incidencia de nefrotoxicidad es de 2 por ciento y es usualmente leve y reversible. El daño vestibular es más frecuente y de más importancia clínica aunque también es reversible. Tanto la dosis como la duración del tratamiento parecen ser responsable de la nefrotoxicidad. Su dosificación debe modificarse de la siguiente manera: con depuraciones de creatinina sobre 70 cc/min, debe administrarse 80 mg cada 8 horas, de 30 a 69 cc/min, debe administrarse 80 mg cada 12 horas y con depuraciones de creatinina bajo 29 cc/min debe administrarse 80 mg cada 48 horas. El esquema que se ha presentado es solo un guía de ayuda en el tratamiento. La información es incompleta y en muchos casos sujeta a cambios futuros. No está justificado el privar a estos pacientes del beneficio que estas nuevas drogas ofrecen.

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THE 1969 SCHISTOSOMIASIS SKIN TEST SURVEY IN PUERTO RICO

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In 1964 Kagan and co-workers conducted a program of schistosomiasis skin testing of fifth-grade school children throughout Puerto Rico (1). Their study delineated the geographic variations in prevalence of positive reactors and, presumably, of infection with schistosomiasis at that time. By 1969, after several pilot control projects, the Puerto Rico Health Department was preparing to initiate a program of snail control, beginning in the areas of greatest schistosomiasis prevalence. The Health Department required a more current appraisal of the patterns of prevalence of schistosomiasis to help determine the areas of highest priority for control. This paper reports the results of a skin test survey conducted in 1969 in a manner similar to the 1964 survey.

Materials and Methods

The geographic bases for the 1969 survey were the same 31 watershed areas defined in the 1964 survey (1). These areas generally conform to major stream drainage basins of Puerto Rico, with Vieques Island a separate watershed.

The population studied consisted of a sample of all fifth-grade public school students within each watershed. We employed a random cluster sampling technique, similar to the one used in 1964 (1) to select fifth-grade classroom units for skin testing. Schools listed as "urban" and "rural" by the Department of Education were sampled separately.

For the eastern half of the Island, we selected the same schools that were studied in 1964. If the school no longer existed, we tested the school which the Department of Education designated as corresponding to the original school. In the western part of the Island and in metropolitan San Juan, percentages of positives in 1964 were low, and the original sample was larger than that required for statistical purposes. We therefore recalculated the required sample size using the formula employed in 1964. We then selected the new sample

from the schools previously studied, but randomly excluded a number of schools to reduce the sample to the appropriate size.

Adult *Schistosoma mansoni* antigen was prepared with a nitrogen content of 35-40 micrograms per milliliter (2). Using a tuberculin syringe, we injected 0.5 ml of antigen intradermally into the volar aspect of the forearm of each subject. Fifteen minutes later the wheal induration was outlined with a ball point pen and was transferred to a paper moistened with alcohol. The transcribed wheal area was measured using a transparent template, as described by Pellegrino and Macedo (3). Control fluid was injected into each subject as part of a research program, but the control wheals were not used to interpret the test results reported in this paper.

The criteria for interpreting the tests were those determined for the Puerto Rican population (4). For males under 14 years of age and for all females, an antigen wheal area of 1.0 cm² or greater indicated a positive reaction. For males age 14 and over, an antigen wheal 1.2 cm² or greater was considered positive.

The test results were recorded on a form which served both as a permission slip and questionnaire for demographic information. These forms were coded by hand, and the data was processed using a digital computer.

Results

The skin test was positive in 13.6 percent of the 9,365 children tested. Of the male children, 17.3 percent were positive as compared to 9.7 percent for females.

Children attending schools in urban areas were as likely to have positive skin tests as those from rural schools. In urban schools, 14.5 percent of the children reacted positively; in rural schools, 12.2 percent had positive reactions.

The number of males and females tested were about equal in each watershed and the age distribution varied little from one watershed to another. The watersheds are ranked by percentage of positive reactors (Table I). In each of watersheds 02, 05, 06, and 07, the results from one or two schools are not tabulated due to an error in data collection. In all cases these were rural schools which had high rates of skin test reactors in 1964. A map of Puerto Rico depicting prevalence of positive reactors by watershed (Figure 1) shows a pattern of maximum skin test reactivity in the south-eastern and eastern parts of the Island.

Contribution of the San Juan Tropical Disease Laboratories, Ecological Investigations Program, Center for Disease Control, Health Services and Mental Health Administration, Public Health Service, U. S. Department of Health, Education, and Welfare, San Juan, Puerto Rico, 00936.

TABLE I: RANKING OF WATERSHEDS BY PREVALENCE OF POSITIVE SKIN TEST REACTORS FOUND IN RANDOM SAMPLE OF FIFTH-GRADE CHILDREN OF BOTH SEXES, PUERTO RICO, 1969

Rank	Watershed Number	Principal Towns in Watershed	Number Tested	Number Positive	Percent Positive
1*	07	Yabucoa, Maunabo	358	99	27.7
2*	06	Humacao	289	75	26.0
3*	05	Gurabo, Juncos, Las Piedras	316	74	23.4
4	25	Upper Yauco, Castañer	85	17	20.0
5	22	Utuado, Jayuya, Adjuntas	433	86	19.9
6	14	Guayama, Salinas	649	128	19.7
7	12	Comerio, Barranquitas, Aibonito	502	86	17.1
		Cidra, Cayey			
8	13	Patillas, Arroyo	503	84	16.7
9	18	Toa Alta, Naranjito	252	39	15.5
10	08	San Lorenzo, Caguas, Aguas Buenas	482	74	15.4
11	01	Fajardo, Ceiba	180	27	15.0
12	03	Naguabo	198	29	14.6
13	23	Ponce	310	44	14.2
14*	02	Río Grande, Luquillo	256	35	13.7
15	04	Trujillo Alto, Carolina, Loíza	320	40	12.5
16	09	San Juan, Río Piedras	427	51	11.9
17	21	Arecibo	279	29	10.4
18	31	Vieques	169	17	10.1
19	15	Villalba, Juana Díaz, Coamo, Santa Isabel	402	38	9.5
20	24	Yauco, Guayanilla, Peñuelas	300	28	9.3
21	29	Hormigueros, Cabo Rojo, San Germán, Maricao, Sabana Grande	295	27	9.2
22	19	Dorado, Toa Baja, Vega Baja, Vega Alta, Corozal, Morovis	319	29	9.1
23	16	Orocovis	203	17	8.4
24	30	Lajas, Ensenada, Guánica	165	12	7.3
25	27	Añasco, Las Marías	213	13	6.1
26	10	Bayamón, Cataño, Guaynabo	312	19	6.1
27	26	Aguadilla, Rincón, Lares, Hatillo, Moca, Aguada, Isabela, Quebradillas, San Sebastián, Camuy	421	24	5.7
28	28	Mayagüez	236	13	5.5
29	17	Ciales	170	8	4.7
30	11	Upper Bayamón	111	5	4.5
31	20	Barceloneta, Manatí	210	9	4.3
TOTAL -			9365	1276	13.6

* - Study sample not completed because of error in data collection.

Discussion

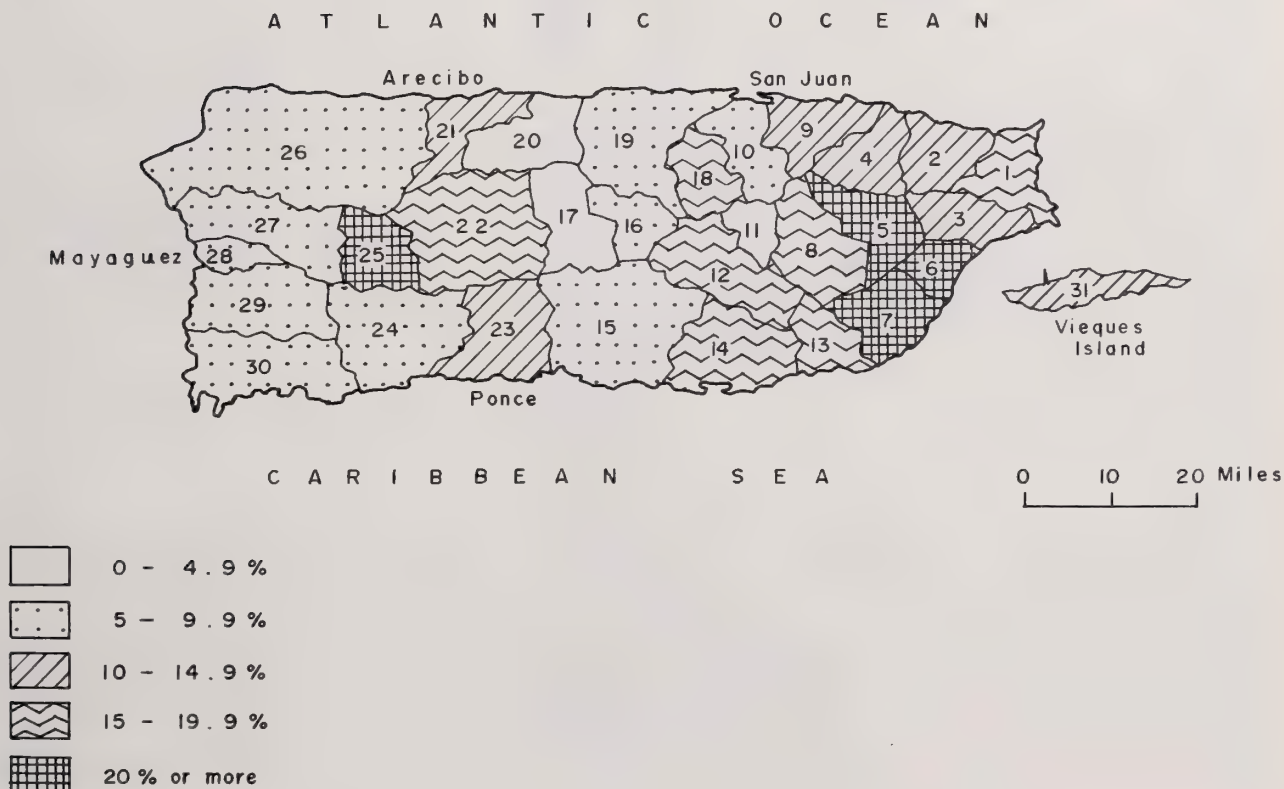
In 1964 the skin tests were done on the back rather than on the forearm, and a different set of criteria was used, based on both antigen and control wheal sizes. The changes we have made in method of performing and reading the test considerably reduce the time and

expense of a skin test survey, with little loss in accuracy (4). However, these departures from the method used by Kagan *et al* hinder direct comparison of the 1964 and 1969 data.

The geographic distribution of schistosomiasis skin test positives found in this study is the same as that noted previously. The area of greatest prevalence is in

FIGURE 1

SCHISTOSOMIASIS PREVALENCE RATES BY WATERSHED AREA
FOUND IN RANDOM SAMPLE SKIN TEST SURVEY OF 9,365 FIFTH
GRADE CHILDREN OF BOTH SEXES, PUERTO RICO, 1969



the Juncos, Las Piedras, Yabucoa, Humacao region, with relatively high prevalences throughout the eastern third of the Island. The inadvertent deletion of about 10 percent of the sample in watersheds 02, 05, 06, and 07 should not materially affect the results from these areas.

The watersheds in western Puerto Rico had lower prevalences, with the exception of watershed 25, which had 20 percent positive reactors. Although this value is based on a sample of only 85 children, the area may represent a focus of schistosomiasis not recognized previously.

Males in Puerto Rico are considerably more likely to be positive to the schistosomiasis skin test than are females, perhaps reflecting greater exposure to *S. mansoni*-infected water. Males tend to react more vigorously to intradermal tests in general (4, 5, 6) and this fact

may exaggerate the difference in prevalence of positives for the two sexes.

Nearly equal rates of skin test reactivity among children from urban and rural schools were observed in 1964 and in this survey. Children living in rural barrios may attend school in urban areas, and the schools designated as urban are often in small municipalities which are not urban in the usual sense. Despite these inaccuracies in classification, our survey results indicate that the concept of schistosomiasis as a rural disease in Puerto Rico is not a valid one.

In summary, the schistosomiasis skin test is admittedly an insensitive test with many false negative reactions in children, and it does not aid in clinical diagnosis (2). Nevertheless, the test is a useful and rather inexpensive method for determining areas of relatively high schistosomiasis prevalence within a geographic area. This infor-

mation can then be used to direct a control program to areas of greatest endemicity. Based on the results presented here, the Puerto Rico Health Department is initiating snail vector control in southeastern Puerto Rico.

Summary

Adult *Schistosoma mansoni* antigen was used in a 1969 skin test survey to delineate the geographic distribution of schistosomiasis in Puerto Rico. The population studied, 9,365 fifth-grade school children, was selected and tested in a manner similar to that followed in a 1964 survey and was representative of the entire Island. Positive skin test reactions were found in 13.6 percent of the children tested, with a higher percentage of males (17.3 percent) reacting positively than females (9.7 percent). Positivity rates did not differ significantly in children attending urban as compared to rural schools. A prevalence map, based on 31 watershed units, showed a pattern of maximal skin test reactivity in the southeastern and eastern part of the Island. This information is being used by the Puerto Rico Health Department to establish priorities for control activities. Methodological differences between the 1964 and 1969 surveys hinder direct comparison between them.

Resumen

Antígeno preparado con gusanos adultos de *Schistosoma mansoni*, fue utilizado para hacer pruebas intradermales en un estudio hecho en el 1969, para delinear la distribución geográfica de bilharzia en Puerto Rico. La población utilizada, 9365 niños de quinto grado, fue seleccionada y examinada en una manera similar a aquella usada en la encuesta de 1964 y fue representativa de toda la Isla. Reacciones positivas de la piel fueron encontradas en 13.6 por ciento de los niños examinados

con un porcentaje positivo más alto en varones (17.3 por ciento) que en hembras (9.7 por ciento). No se vio diferencia significativa en la comparación de positividad entre los niños de escuelas urbanas y rurales. Un mapa de prevalencia basado en 31 unidades de cuencas de agua, demuestra un patrón de reacción máxima a pruebas cutáneas en el este y sureste de la isla. Esta información está siendo utilizada por el Departamento de Salud de Puerto Rico, para establecer prioridades en las actividades de control. Diferencias en métodos usados en las encuestas del 1964 y 1969 evitan se pueda hacer una comparación directa entre ambos.

Acknowledgments

Our thanks to Mr. Juan R. Palmer, Chief, Vector Control Section, Puerto Rico Health Department, and the field crews of the Puerto Rico Health Department's Bilharzia Control Program for their help in carrying out this study. Special acknowledgment and thanks to Dr. Henry Negrón Aponte for his aid and consultation during the course of the study.

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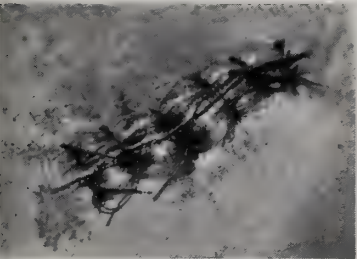
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Warnings: Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired. Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (> 5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities. Accordingly, check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently — both can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides

are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in postsympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Rarely, necrotizing vasculitis, paresthesias, icterus, pancreatitis, and xanthopsia have occurred with thiazides alone.

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CARTAS AL EDITOR

Carta al Editor

Boletín Asociación Médica de Puerto Rico

Apartado 9387

Santurce, Puerto Rico 00908

Señores:

El Doctor Sifontes, Editoralista sobre las indicaciones para amigdalectomía (Vol. 65 - Abril '73 No. 4) y concurro con él de que este procedimiento se hace más de lo que está justificado. Si tengo que diferir sobre lo relacionado al factor inmunológico, pues en la literatura hay suficiente información para justificar el lado que uno desee defender. Me permito citar el texto de Otorinolaringología de Paparella y Shumrick (W. B. Saunders 1973) Vol. 1 - Capítulo 29 - Basic Principles of Immunology, pag. 725.

"Reasonable indications for tonsillectomy and adenoidectomy include eustachian tube or upper airway obstruction from pharyngeal lymphoid tissues. The recent appreciation of gut-associated lymphoid tissues as playing important roles in controlling differentiation and final expression of the immunoglobulin-producing cell lines has led to speculation that the tonsils might function as central lymphoid tissue (Peterson et al. 1965). No clear evidence exists that an immune deficiency results from tonsillectomy, however. The central controller of the immunoglobulin system in man would seem to be more widespread in distribution, unlikely that removal of tonsils (or appendices or intestinal resections for that matter) can measurable affect the immunoglobulin production apparatus. Furthermore, peripheralization of the competent cells allows postnatal removal or ablation of central tissues with minimal effects in most cases." (Peterson, R. D. A., Cooper, M. D. and Good R. A. Amer. J. of Med. 38: 579-604, 1965).

Hay también que apuntar que a Stool se le olvidó mencionar el hecho de que son muchas más las veces que el estado de las amígdalas y adenoides interfiere con la fonación, que las veces que el removerla le afecta. Es necesario apuntar que aquellos niños con uvula bifida y paladar hendido submucosal (submucous

cleft palate) no se debe de remover las adenoides ya que ellas sirven el propósito de llenar la nasofaringe y ayudar en la fonación. El hacerlo conlleva producirle una cualidad nasal (rinolalia) al paciente.

Podemos ayudar a reducir el número de procedimientos innecesarios no sólo como sugiere Sifontes, a nivel de los hospitales, sino ampliando la educación sobre otorinolaringología en nuestra Escuela de Medicina y a través de cursos o presentación de estos problemas en las diferentes actividades educativas que se ofrecen — donde la otorinolaringología recibe muy poca atención.

Por último me permito recordar que el problema de las amígdalas y adenoides se asemeja al de la úlcera péptica que por razones económicas es mejor operar que tener que recurrir al médico 4 a 7 veces por año, por varios años a recibir la terapia indicada.

Muy atentamente,

Enrique A. Vicéns, MD

Jefe Sección ENT y Bronco-Esofagología
Hospital Distrito de Ponce

To the Editor:

Question:

When did the Federal and State Governments acquire or assume, the right to require physician's services "ad honorem", for non-medical functions at that?

Answer:

When the Social Security Administration decreed by fiat that all hospitals must have Utilization Committees, in order to care for Medicare beneficiaries under the law.

Why should physicians have to give of their time for the purpose of policing hospital utilization? If the Social Security Administration (S. S. A.) believes it is being bilked by hordes of physicians who cause overutilization, then let S. S. A. do the policing. Department

stores and other businesses subject to shop-lifting hire special agents to perform surveillance functions; why should not the S. S. A. do the same? The cost of such surveillance is properly part of the operating cost of the party that can expect to benefit from the service rendered in this case, the S. S. A.

And now, our Health Department is trying to require that the utilization committees not only review Medicare cases, but those admitted under various private insurance plans as well, such as Blue Cross and S. S. S. What reasoning can possibly justify performing such work, with no recompense, for the sole benefit of a private insurance company? Let them send their own inspectors to review hospital charts, if they fear over-utilization. Let their employees be the ones to let the

doctor and patient know that the company is considering not paying the hospital bill after a certain date. T There is no justification at all for having physicians, not employed by the insurance companies (including S. S. A.) nor even the hospital, as inspectors to check on how long their fellow physicians keep patients in the hospital. Nor should this be an expense for the hospitals, as it is in some jurisdictions, in which the hospitals pay the Utilization Committees members a nominal fee for their time. It is the insurance companies that benefit, so let them pick up tab.

Max Ramírez de Arellano, MD

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Me alegro de saber que ya eres médico. Te graduaste de una buena escuela, y, habiendo hecho tu internado y pasado la reválida, ya has empezado a trabajar en tu pueblo. Enhorabuena.

Hasta ahora has sido un estudiante. Te mandaban. Te decían cómo hacer las cosas, te guiaban. Ahora estás por tu cuenta, y de pronto te has convertido en una “autoridad”; una persona a quien todos consultan, un líder del pueblo.

Estás pasando por la etapa más peligrosa de tu carrera: peligrosa para ti y para todos los que te rodean; porque tus compueblanos te están haciendo creer que lo sabes todo, cuando todavía estás empezando a aprender. Te dicen “doctor”, que es como decirte “sabio”, y eso te halaga. Las circunstancias tienden a hacerte vanidoso. ¡Mantente en guardia! Un médico vanidoso es un médico peligroso. La vanidad es el peor de los consejeros.

Necesitas humildad. La vas a necesitar hasta el último día de tu vida. Lo primero que tienes que hacer es confesarte contigo mismo; darte cuenta exacta de lo poco que sabes, y buscar la ayuda de los que saben más que tú. Tienes que aprender a decir “no sé”. Tienes que aprender a decir: “Necesito consultar con alguien que sepa de esto más que yo”. Si no aprendes eso ahora que estás empezando, no lo aprenderás nunca, y el no aprenderlo te habrá de causar infinitas angustias.

Ser médico es algo más que tener un título. Es seguir una noble y exigente tradición. Esta profesión a que tú ahora perteneces se ha impuesto a sí misma rigurosas normas a través del tiempo. Se ha distinguido ante todo por su incesante búsqueda de la verdad; por haberse negado a transigir con el engaño. Ha amparado la vida en todas las circunstancias; y, en medio de la guerra, ha curado las heridas del enemigo, imponiendo la Ley de Dios por encima del desgobierno de los hombres.

Ahora empiezas tu vida profesional con un prestigio que todavía no te has ganado. Es el prestigio que tu profesión ha levantado, a través de los siglos, como un altar en el corazón de la humanidad. Por ser médico todo el mundo te mira con respeto, y espera que, además de ser hábil, seas honrado, decente, veraz. No serlo, o serlo a medias solamente, sería traicionarte a ti mismo; traicionar a tu profesión y defraudar a la sociedad.

La sociedad ha de exigirte mucho, por lo mismo que te aprecia mucho. Tu vida de ahora en adelante no va a ser fácil. Tendrás que estudiar constantemente, y nunca acabarás de estudiar. Tendrás que sufrir las penas propias y las ajenas. Tendrás que trabajar más, y divertirti menos, que la mayoría de los hombres.

¿El premio? El mejor premio a esta vida de sacrificios no ha de ser en dólares. Será en respeto y cariño. Será en el homenaje silencioso de una sociedad agradecida. Será en legar a tus hijos; y a tus nietos, lo mejor que se puede legar: un nombre que les sirva de orgullo.

Entre tu edad y la mía hay una distancia de cincuenta años. A través de ese espacio de tiempo, y en nombre de una generación de médicos que ya ha rendido su labor, te extiendo un saludo de bienvenida fraternal.

José Rodríguez Pastor, M. D.

DISABILITY INSURANCE UNDER SOCIAL SECURITY

Whenever a physician is asked to furnish a medical report in connection with a patient's claim for social security disability benefits, it's a reminder that social security is not just for the retired—it also provides important financial help for people who cannot work because of a serious illness or injury. Currently, over 3 million men, women and children receive social security disability checks every month \$5 billion a year. In addition, more than 76 million working men and women are insured for disability benefits as a result of their earnings—wages or self-employment—under social security. Beginning July 1, 1973, full Medicare protection will be extended to persons under age 65 who for at least 24 consecutive months have been receiving monthly social security benefits because they are disabled.

A person under 65 can receive monthly disability benefits if he has a physical or mental impairment severe enough to prevent him from doing any substantial gainful work for a year or longer. Benefit amounts based upon a person's earnings under social security range from \$84.50 to \$345.50 a month for the disabled worker alone, and the maximum monthly benefit for a disabled worker with a family is \$620.40.

Everyone who applies for disability benefits—whether he subsequently receives monthly benefits or not—is referred for possible services to his State vocational rehabilitation agency. Such services include counseling, teaching new employment skills, training in the use of prostheses, and job placement.

These services are generally provided from State Federal appropriations. In some cases, however, social security pays the cost of rehabilitating disabled beneficiaries.

From a Small Beginning

The original Social Security Act of 1935 provided benefits only for the retired worker. It was not until 1954 when the disability "freeze" provision was added that the law gave some protection to the disabled worker. Under the freeze, years when a worker earned little or nothing because of disability were not counted against him later in deciding if he was eligible for retirement benefits, or in figuring his retirement benefit amount. To be eligible for the freeze, the worker had to have a disability that was expected to be of "long-continued and indefinite" duration.

Two years later, monthly cash benefits were provided for disabled workers aged 50 to 64, and also for the disabled adult sons and daughters of retired or deceased worker if the son or daughter had been continuously disabled since childhood.

Over the years, the program has been further improved. The minimum age limit of 50 for payment or benefits to disabled workers was eliminated; "long-continued and indefinite" duration was changed so that an insured worker could be eligible if his disability had lasted or could be expected to last for at least 12 months; fewer years of covered employment were required for a young worker to be insured for disability; and benefits were provided for disabled widows (between ages 50 and 60) of covered wage earners. The latest change is, of course, Medicare protection for disabled persons under 65.

Who Can Get Benefits?

Social security disability benefits can now be paid for

**A disabled worker under 65 and his family, if he has worked under social security for a certain length of time, ordinarily 5 of the 10 years preceding the onset of disability. (Special provisions apply to workers disabled by blindness allowing them to qualify with even less work under the program.) For the worker who becomes disabled before he reaches 31, the work requirement*

ranges down with age to as little as 1 1/2 years.

**A person continuously disabled since childhood (before age 22), if one of his parents (in some cases a grandparent) who is covered under social security retires, becomes disabled, or dies. The mother of the disabled son or daughter may also receive monthly benefits as long as she has the child in her care.*

**A disabled widow 50 or over, if her late husband was covered under social security, and if she meets the specified level of medical severity. This also applies to disabled dependent widowers and certain disabled surviving divorced wives.*

Reporting Medical Evidence

When a patient applies for benefits, he is asked to submit medical evidence to support his claim. This evidence usually consists of data from the records of his treating physician, clinic or other medical source. Our experience with the disability program in Puerto Rico indicates that in about three out of five cases no further medical development is needed because the treating source already has enough information on record to provide a good picture of the applicant's condition and how it limits his ability to work. This information may be requested on the patient's behalf by a social security office—or, more often, by the Program of Disability Determination. This is the full name of the agency in Puerto Rico that evaluates social security disability claims for Puerto Rico residents. Like other State agencies throughout the country that work with Social Security in the disability insurance program our State Agency in Puerto Rico includes both physicians and trained disability examiners on its professional staff. They form a balanced team of medical and non-medical people who can handle anything from a strictly medical issue to a complete assessment of the vocational factors which bear on the disability decision.

With the assistance of our staff of reviewing physicians, we endeavor to make these requests for medical information relate as directly as possible to the condition which the claimant states is the cause of his disability. The goal of the individually tailored request is to ease the medical reporting burden of the busy physician or clinic, without jeopardizing the claimant's right to have his case decided on the basis of all relevant information available.

The evaluating physician here in the State Agency never sees the patient. He depends heavily on information supplied by the physician or clinic to assess the severity of the applicant's impairment, its expected duration and the extent of his residual functional capacity. The disability decision, therefore, rests largely on the quality of the medical evidence obtained. A detailed report from the treating source, including objective findings and laboratory procedures, will usually be sufficient for us to evaluate the claim and make a decision.

For example, if the patient experienced a myocardial infarction, we would look to the report submitted by the treating source of such information as date of occurrence, place and duration of the hospitalization, as well as results of X-rays, electrocardiograms, and other laboratory studies. Serial ECG tracings should, whenever possible, accompany the report so that our staff of physicians may also have the benefit of reviewing this essential documentation. Equally important is the medical history, including onset of chest discomfort, relationship to effort, intensity, location, radiation, regularity, and to what extent relief is obtained by rest or medication.

If a report does not contain all the findings necessary to make a proper decision, one of our reviewing physicians may recontact the medical source. However, the additional time required may delay the patient's claim and can add up to a significant additional program expense.

You can help speed the decision on your patient's claim by reporting all relevant data about his medical condition as promptly as possible. Establishing the onset date of disability—often a key factor

in determining the beginning date and amount of the claimant's benefits—is frequently difficult. Therefore, it is extremely helpful if the reporting physician includes the date of each important fact or finding. To save time, he may enclose photocopies of pertinent sections of the patient's chart or of hospital or consultant's reports.

Criteria for Evaluating Disability

In making disability determinations, our agency uses medical criteria developed by the Social Security Administration to insure uniform evaluation of all applicants no matter where they live, and to help simplify and speed the decision process. These criteria were worked out with the aid of practicing physicians, major medical organizations and SSA's Medical Advisory Committee.

Generally, a claimant who is not working can meet the social security definition of disability if he has an impairment or combination of impairments that are the same as, or medically equivalent to, any set of findings in the criteria. (This is the only way the **widow 50 or over** can qualify for disability benefits.) However, for **all other claimants** whose impairments fall short of this test, such factors as age, education, and work experience added to the functional limitations imposed by the medical condition are taken into consideration in making the disability decision.

The complete criteria, including the medical findings listed by body system, are contained in a handbook designed especially for professionals who come in contact with the disabled population. The handbook describes impairments in terms of specific symptoms, signs and laboratory findings that are presumed to be severe enough to prevent a person from working for a year or longer.

The handbook may be obtained from Disability Determination Program, Ramos Oller Building, 1503 Asia Street, Santurce, Puerto Rico, 00909 - Telephone, 725-0260. We also welcome any inquiries from physicians who wish to know more about the social security disability program and its policies and procedures.

Jaime F. Pou, MD

INDICE DE ANUNCIANTES

1. Burroughs Wellcome - Empirin Compound \bar{c} Codeine
2. Ciba Pharm. - Vioform HC
3. Geigy Pharm. - DBI-TD
4. Pharm. Labs. - Institutional
5. Roche - Dalmane, Efudex, Librium, Valium
6. Rorer - Ascriptin
7. Searle - Pro-Banthine
8. Smith, Kline & French - Dyazide



Classic flu management

Only Maalox[®] has been added to help protect the intolerant

Ascriptin is for those patients who suffer from gastric intolerance due to aspirin. One Ascriptin tablet combines 150 mg. of Maalox with 5 grains of aspirin to help reduce aspirin-induced gastric distress. When the symptoms of flu occur, specify Ascriptin . . . classic flu management—improved.



Ascriptin[®]—the Maalox[®]-protected aspirin



WILLIAM H. RORER, INC.
FORT WASHINGTON, PA. 19034

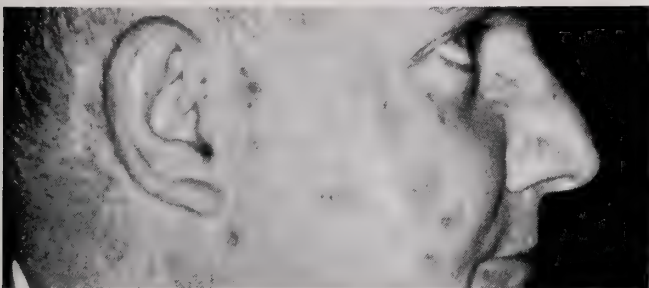
**What's
on your
patient's
face...**

**may be more important than
his chief complaint**

The lesions on his face may be solar/actinic — so-called ‘senile’ keratoses...and they may be premalignant.

Solar, actinic or senile keratoses

These lesions may be called by several names, but they usually can be identified by the following characteristics: the typical lesion is flat or slightly elevated, of a brownish or reddish color, papular, dry, rough, adherent, and sharply defined. They commonly occur as multiple lesions, chiefly on the exposed portions of the skin.



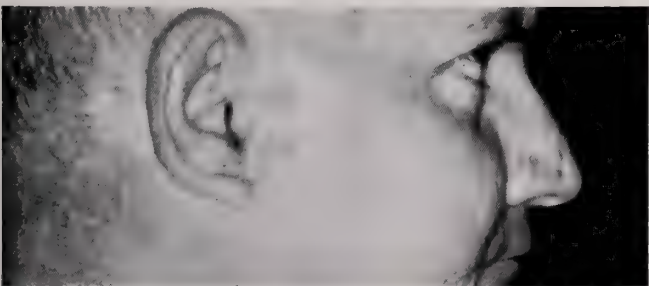
Patient P.T. seen on 3/29/67 shows typical lesions of moderately severe keratoses. Note residual scarring on ridge of nose from previous cryosurgical and electro-surgical procedures.*

Sequence of therapy/ selectivity of response

After several days of therapy with Efudex® (fluorouracil), erythema may begin to appear in the area of the lesions; the reaction usually reaches its height of unsightliness and discomfort within two weeks, declining after discontinuation of therapy. This reaction occurs in affected areas. Since the response is so predictable, lesions that do not respond should be biopsied.

Acceptable results

Treatment with Efudex provides highly favorable cosmetic results. Incidence of scarring is low. This is particularly important with multiple facial lesions. Efudex should be applied with care near the eyes, nose and mouth.



Patient P.T. seen on 6/12/67, seven weeks after discontinuation of 5%-FU cream. Reaction has subsided. Residual scarring not seen except for that due to prior surgery. Inflammation has cleared and face is clear of keratotic lesions.*

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Multiple actinic or solar keratoses.

Contraindications: Patients with known hypersensitivity to any of its components.

Warnings: If occlusive dressing used, may increase inflammatory reactions in adjacent normal skin. Avoid prolonged exposure to ultraviolet rays. Safe use in pregnancy not established.

Precautions: If applied with fingers, wash hands immediately. Apply with care near eyes, nose and mouth. Lesions failing to respond or recurring should be biopsied.

Adverse Reactions: Local — pain, pruritus, hyperpigmentation and burning at application site most frequent; also dermatitis, scarring, soreness and tenderness. Also reported — insomnia, stomatitis, suppuration, scaling, swelling, irritability, medicinal taste, photosensitivity, lacrimation, leukocytosis, thrombocytopenia, toxic granulation and eosinophilia.

Dosage and Administration: Apply sufficient quantity to cover lesion twice daily with non-metal applicator or suitable glove. Usual duration of therapy is 2 to 4 weeks.

How Supplied: Solution, 10-ml drop dispensers — containing 2% or 5% fluorouracil on a weight/weight basis, compounded with propylene glycol, tris(hydroxymethyl)aminomethane, hydroxypropyl cellulose, parabens (methyl and propyl) and disodium edetate.

Cream, 25-Gm tubes — containing 5% fluorouracil in a vanishing cream base consisting of white petrolatum, stearyl alcohol, propylene glycol, polysorbate 60 and parabens (methyl and propyl).

**This patient's lesions
were resolved with**

Efudex[®]
(fluorouracil)
5% cream/solution
...a Roche exclusive



Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, N.J. 07110

*Data on file, Hoffmann-La Roche Inc., Nutley, N.J.

NOTICIAS

PROGRAMA CONTROL ENFERMEDADES VENEREAS

NUEVO PROGRAMA DE GONORREA

El Programa de Enfermedades Venéreas de la Secretaría Auxiliar para Servicios Médico Preventivos del Departamento de Salud ya comenzó el nuevo programa con el propósito de intensificar los esfuerzos en el control de gonorrea. Aunque las estadísticas revelan un descenso en el informe de gonorrea durante los últimos tres años, la prevalencia actual y verdadera no se conoce ya que el énfasis en el control de gonorrea se había minimizado.

A todos los proveedores de salud que llevan a cabo exámenes cervicales a las mujeres en edad de gestación, se les pide que le hagan cultivos, tanto cervicales como rectales cuando sea posible. Se estima que existe una gran reserva de mujeres asintomáticas-aproximadamente 85 por ciento de las mujeres infectadas no tienen manifestaciones.

El Programa Control de Enfermedades Venéreas proveerá los siguientes recursos a todos los médicos que deseen hacer un examen rutinario a las mujeres a quienes se les practique exámenes pélvicos:

1. Medios de cultivos de GC (Thayer-Martin y Transgrow)
2. Proceso de laboratorios para los cultivos
3. Recolección y distribución de cultivos en el área metropolitana de San Juan a los laboratorios. (Para el área de la isla se distribuirá el Transgrow a los laboratorios por medio del sistema postal).
4. Probenecid y Penicilina Procinada Acuosa
5. Asistencia epidemiológica en cada caso reportado de gonorrea en el hombre.

Todos los interesados se pueden comunicar con el Sr. Salvador A. Mier, Director del Programa Control Enfermedades Venéreas por los teléfonos 782-3231 o 781-2525 Ext. 215.

INFORME DE CASOS DE VENEREAS

Es de extrema importancia que todos los casos de enfermedades venéreas sean reportados al Departamento de Salud con el propósito de aplicarles la epidemiología. Recientemente el informe de la Comisión Nacional de Enfermedades Venéreas declaró que "Uno de los serios problemas en el control de estas enfermedades los constituye la falla de parte de los médicos practicantes al no informar a las Autoridades de Salud todos los casos de enfermedades venéreas diagnosticados y tratados".

La epidemiología ha probado contribuir bastante al éxito en el control de las enfermedades venéreas. Sin embargo, para alcanzar la efectividad que la situación exige se hace imprescindible contar con la completa cooperación de la comunidad médica. A los efectos de que nuestro programa alcance un grado de excelencia en la realización de su tarea, se hace necesario contar con la más decidida cooperación de ustedes, médicos, con los epidemiólogos asignados a su área y que consideren los servicios epidemiológicos como una extensión de su oficina, los cuales pueden utilizar tan pronto como se les presente un caso de sífilis infecciosa. Para disminuir el riesgo de la propagación de estas enfermedades, recomendamos informar los casos mediante llamada telefónica por el 782-3231 o 781-2525 ext. 215. Esta información se mantendrá en la más estricta confidencialidad.

Deseamos informarles que nuestro Programa les ofrece además, el servicio de examen a campo oscuro "Darkfield" cuando les sea necesario para el diagnóstico de estas enfermedades. Nuestros Técnicos en Epidemiología están debidamente adiestrados y capacitados para llevar a cabo esta tarea.

Trabajando todos en conjunto podemos reducir a un mínimo la incidencia de las enfermedades venéreas en Puerto Rico.

**Cuando comen lo que les gusta
y no lo que deben...**



ayude a cubrir "el déficit" de vitaminas con

Unicap Therapeutic

10 vitaminas combinadas con 7 minerales

Cada tableta contiene:

Vitamina A	1.5 mg.
Vitamina D	10 mcg.
Mononitrato de Tiamina (B-1)	10 mg.
Riboflavina (B-2)	10 mg.
Acido Ascórbico (C) (como ascorbato de sodio)	300 mg.
Niacinamida	100 mg.
Clorhidrato de Piridoxina (B-6)	2 mg.
Pantotenato de Calcio	20 mg.
Cobalamina (B-12) (como concentrado de cobalamina)	20 mg.
Vitamina E	30 Unidades Internacionales
Hierro (a partir de 50 mg. de sulfato ferroso)	10 mg.
Yodo (como yoduro de potasio)	0.15 mg.
Calcio (como carbonato)	50 mg.
Cobre (como sulfato)	1 mg.
Manganeso (como sulfato)	1 mg.
Magnesio (como sulfato)	6 mg.
Potasio (como sulfato)	5 mg.

Posología: Adultos y niños mayores de 6 años - 1 tableta diaria.

Presentación: Frascos de 30 y 90

Upjohn

PR 5226.1 MAY, 1969

6811 MARCA REGISTRADA EN E.U.A.: UNICAP THERAPEUTIC

UPJOHN INTER-AMERICAN CORPORATION / CAPARRA / PUERTO NUEVO

How strong must a tranquilizer be for severe anxiety?

As strong as Librium® 25 mg (chlordiazepoxide HCl)



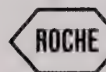
The achievement of desired therapeutic results is often a function of the dosage strength as well as the drug's intrinsic action. Thus, when anxiety is *severe*, the 25-mg strength of Librium frequently provides the necessary antianxiety action with a minimum of unwanted adverse reactions. Librium 25 mg is a convenient dosage form for the relief of severe, incapacitating anxiety, specifically formulated to supplement your counsel and reassurance.

Benefits-to-risks ratio permits higher dosage

For over 13 years, Librium has been recognized for its excellent benefits-to-risks ratio, an asset in the *higher* dosage ranges as in more common clinical applications. Thus, the frequency of dosage with Librium 25 mg can be flexibly adjusted to the needs and response of the individual patient, up to 100 mg daily if required. Total daily dosage for the elderly and debilitated should not exceed 20 mg. When severe anxiety has been reduced, Librium dosage should be correspondingly reduced or discontinued entirely.



basic support
in severe anxiety
Librium® 25 mg
(chlordiazepoxide HCl)
1 capsule t.i.d./q.i.d.



Roche Laboratories
Division of Hoffmann-La Roche Inc
Nutley, N.J. 07110

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Relief of anxiety and tension occurring alone or accompanying various disease states.

Contraindications: Patients with known hypersensitivity to the drug.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation, or in women of childbearing age requires that its potential benefits be weighed against its possible hazards.

Precautions: In the elderly and debilitated and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

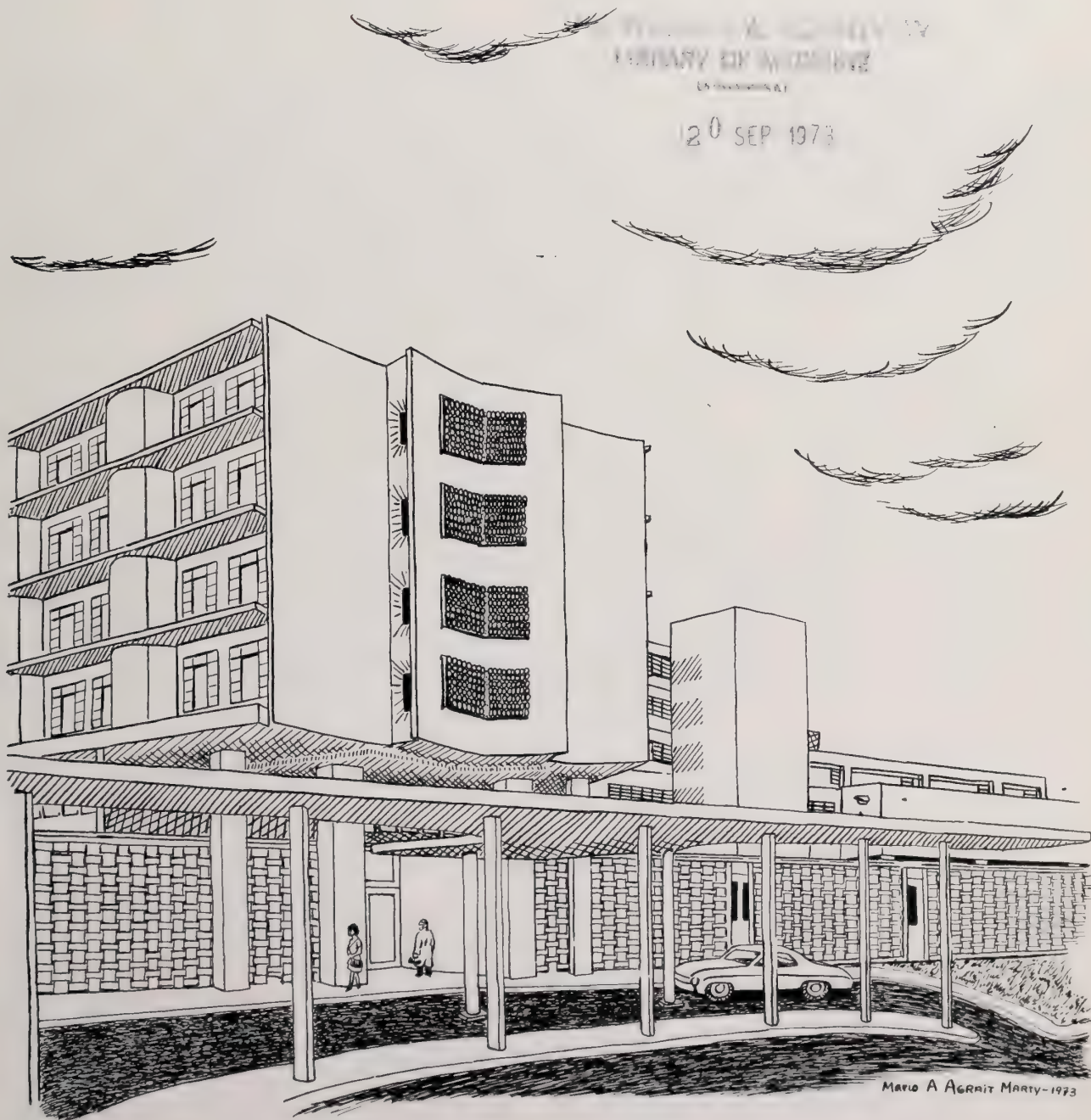
Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

Supplied: Librium® Capsules containing 5 mg, 10 mg or 25 mg chlordiazepoxide HCl. Libritabs® Tablets containing 5 mg, 10 mg or 25 mg chlordiazepoxide.

BOLETIN ASOCIACION MEDICA DE PUERTO RICO

ISPLAY
HELVES

EDICION DEL
CENTRO MEDICO DE MAYAGUEZ



Vol. 65

Agosto 1973

No.8



Everybody experiences psychic tension.



Most people can handle this tension.



Some people develop excessive psychic tension and need your counseling,



and a few may need counseling
and the psychotropic action of Valium® (diazepam).

Before deciding to make Valium (diazepam) part of your treatment plan, check on whether or not the patient is presently taking drugs and, if so, what his response has been. Along with the medical and social history, this information can help you determine initial dosage, the possibility of side effects and the ultimate prospects of success or failure.

While Valium can be a most helpful adjunct to your counseling, it should be prescribed only as long as excessive psychic tension persists and should be discontinued when you decide it has accomplished its therapeutic task. In general, when dosage guidelines are followed, Valium is well tolerated (see Dosage). For convenience it is available in 2-mg, 5-mg and 10-mg tablets.

Drowsiness, fatigue and ataxia have been the most commonly reported side effects.

Until response is determined, patients receiving Valium should be cautioned against engaging in hazardous occupations requiring complete mental alertness, such as driving or operating machinery.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

Dosage: Individualize for maximum beneficial effect.

Adults: Tension, anxiety and psychoneurotic states, 2 to 10 mg b.i.d. to q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed; adjunctively in skeletal muscle spasm, 2 to 10 mg t.i.d. or q.i.d.; adjunctively in convulsive disorders, 2 to 10 mg b.i.d. to q.i.d. **Geriatric or debilitated patients:** 2 to 2½ mg, 1 or 2 times daily initially, increasing as needed and tolerated. (See Precautions.) **Children:** 1 to 2½ mg t.i.d. or q.i.d. initially, increasing as needed and tolerated (not for use under 6 months).

Supplied: Valium® (diazepam) Tablets, 2 mg, 5 mg and 10 mg; bottles of 100 and 500. All strengths also available in Tel-E-Dose® packages of 1000.



Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, N.J. 07110

Valium® (diazepam)

To help you manage excessive psychic tension

the bare facts.

in many dermatoses* the less they wear,
the more they need...

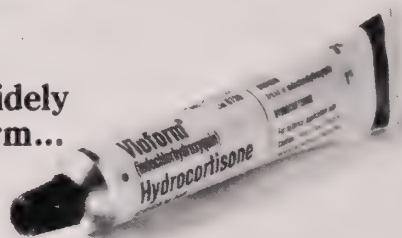
Vioform[®]-Hydrocortisone (iodochlorhydroxyquin and hydrocortisone)

antifungal • antibacterial • anti-inflammatory • antipruritic

Some styles don't leave much to the imagination. And don't provide much cover for common dermatoses, either. Just like plain topical steroids. If the lesion has become infected with fungi or bacteria, plain topical steroids are ordinarily not recommended as sole therapy. Vioform-Hydrocortisone, on the other hand, provides the kind of comprehensive therapy these dermatoses may require. It not only supplies the anti-inflammatory and antipruritic actions of hydrocortisone...but also adds the antibacterial and antifungal actions of Vioform.

*This drug has been evaluated as possibly effective for these indications. See brief prescribing information.

**Another fact...
the most widely
prescribed form...
20 Gm cream**





Vioform®-Hydrocortisone
(iodochlorhydroxyquin and hydrocortisone)

INDICATIONS

Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, FDA has classified the indications as follows:

"Possibly" effective: Contact or atopic dermatitis; impetiginized eczema; nummular eczema; infantile eczema; endogenous chronic infectious dermatitis; stasis dermatitis; pyoderma; nuchal eczema and chronic eczematoid otitis externa; acne urticata; localized or disseminated neurodermatitis; lichen simplex chronicus; anogenital pruritus (vulvae, scroti, ani); folliculitis; bacterial dermatoses; mycotic dermatoses such as tinea (capitis, cruris, corporis, pedis); moniliasis; intertrigo.
Final classification of the less-than-effective indications requires further investigation.

CONTRAINDICATIONS

Hypersensitivity to Vioform-Hydrocortisone, or any of its ingredients or related compounds; lesions of the eye; tuberculosis of the skin; most viral skin lesions (including herpes simplex, vaccinia, and varicella).

WARNINGS

This product is not for ophthalmic use.

In the presence of systemic infections, appropriate systemic antibiotics should be used.

Usage in Pregnancy

Although topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use in pregnant females has not been established. Therefore, they should not be used extensively on pregnant patients in large amounts or for prolonged periods of time.

PRECAUTIONS

May prove irritating to sensitized skin in rare cases. If this occurs, discontinue therapy. May stain.

If used under occlusive dressings or for a prolonged period, watch for signs of pituitary-adrenal axis suppression.

May interfere with thyroid function tests. Wait at least one month after discontinuance of therapy before performing these tests. The ferric chloride test for phenylketonuria (PKU) can yield a false-positive result if Vioform is present in the diaper or urine. Prolonged use may result in overgrowth of nonsusceptible organisms requiring appropriate therapy.

ADVERSE REACTIONS

Few reports include: Hypersensitivity, local burning, irritation, pruritus. Discontinue if untoward reaction occurs. Rarely, topical corticosteroids may cause striae at site of application when used for long periods in intertriginous areas.

DOSAGE

Apply a thin layer to affected areas 3 or 4 times daily.

HOW SUPPLIED

Cream, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearyl alcohol, spermaceti, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of 5 and 20 Gm. **Ointment**, 3% iodochlorhydroxyquin and 1% hydrocortisone in a petrolatum base; tubes of 5 and 20 Gm. **Lotion**, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearic acid, cetyl alcohol, lanolin, propylene glycol, sorbitan trioleate, polysorbate 60, triethanolamine, methylparaben, propylparaben, and perfume Flora in water; plastic squeeze bottles of 15 ml. **Mild Cream**, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a water-washable base containing stearyl alcohol, spermaceti, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of ½ and 1 ounce. **Mild Ointment**, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a petrolatum base; tubes of ½ and 1 ounce.

Consult complete product literature before prescribing.

CIBA Pharmaceutical Company
Division of CIBA-GEIGY Corporation
Summit, New Jersey 07901

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C I B A

BOLETIN

ASOCIACION MEDICA DE PUERTO RICO



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El Boletín se publica mensualmente. El precio de suscripción es de \$10.00 al año. Todo material de anuncio está sujeto a aprobación por la Junta Editora. La tarifa de precios para anuncios será suministrada a solicitud. Copia del anuncio debe ser recibida el día primero del mes que precede al mes de publicación. Representante de anuncios nacionales es la State Medical Journal Advt. Bureau, 1010 Lake St., Oak Park, Ill. 60301.

Podrán ordenarse reimpresos de los artículos a publicarse cuando se reciba notificación de su aceptación.

Trabajos Científicos:

El Boletín acepta para su publicación artículos relativos a medicina y cirugía y las ciencias afines. Igualmente acepta artículos especiales y correspondencia que pudiera ser de interés general para la profesión médica. El artículo, si se aceptara, será con la condición de que se publicará únicamente en esta revista. La AMPR no se hace responsable de las opiniones y declaraciones vertidas por los autores y sus puntos de vista no necesariamente representan aquellos de la AMPR; cualquier relación con la política oficial es coincidencia.

Second Class postage paid at San Juan, P. R.

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CUBIERTA DEL MES DE AGOSTO: CENTRO MEDICO DE MAYAGUEZ



The diabetic
who has
too much...
too much sugar,
too much fat.

Maybe the last thing she needs is more of her own insulin. Especially when you consider that many overweight diabetics already have normal or high levels of endogenous insulin and that insulin is lipogenic.

If she just won't diet and oral therapy is indicated in adult-onset, nonketotic diabetes.

DBI-TD[®] Geigy
phenformin HCl

lowers blood sugar without raising
blood insulin.

For complete details, including dosage,
please read the prescribing information.
It's summarized below.

DBI[®] phenformin HCl
Tablets of 25 mg.
DBI-TD[®] phenformin HCl
Timed-Disintegration
Capsules of 50 and 100 mg.

Indications: Stable adult diabetes mellitus; sulfonylurea failures, primary and secondary; adjunct to insulin therapy of unstable diabetes mellitus.

Contraindications: Diabetes mellitus that can be regulated by diet alone; juvenile diabetes mellitus that is uncomplicated and well regulated on insulin; acute complications of diabetes mellitus (metabolic acidosis, coma, infection, gangrene); surgery or immediately after surgery where insulin is indispensable; severe hepatic disease; renal disease with uremia; cardiovascular collapse (shock); after disease states associated with hypoxemia.

Warnings: Use during pregnancy is to be avoided.

Precautions: 1. **Starvation Ketosis:** This must be differentiated from "insulin lack" ketosis and is characterized by ketonuria which, in spite of rel-

atively normal blood and urine sugar, may result from excessive phenformin therapy, excessive insulin reduction, or insufficient carbohydrate intake. Adjust insulin dosage, lower phenformin dosage, or supply carbohydrates to alleviate this state. **Do not give insulin without first checking blood and urine sugar.**

2. **Lactic Acidosis:** This drug is not recommended in the presence of azotemia or in any clinical situation that predisposes to sustained hypotension that could lead to lactic acidosis. To differentiate lactic acidosis from ketoacidosis, periodic determinations of ketones in the blood and urine should be made in diabetics previously stabilized on phenformin, or phenformin and insulin, who have become unstable. If electrolyte imbalance is suspected, periodic determinations should also be made of electrolytes, pH, and the lactate-pyruvate ratio. The drug should be withdrawn and insulin, when required, and other corrective measures instituted immediately upon the appearance of any metabolic acidosis.

3. **Hypoglycemia:** Although hypoglycemic reactions are rare when phenformin is used alone, every precaution should be observed during the dosage adjustment period particularly when insulin or a sulfonylurea has been given in combination with phenformin.

Adverse Reactions: Principally gastrointestinal; unpleasant metallic taste, continuing to anorexia, nausea and, less frequently, vomiting and diarrhea. Reduce dosage at first sign of these symptoms. In case of vomiting, the drug should be immediately withdrawn. Although rare, urticaria has been reported, as have gastrointestinal symptoms such as anorexia, nausea and vomiting following excessive alcohol intake. (B) 98-146-103-E (6/72)

For complete details, including dosage, please see full prescribing information.

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"Prescription drugs – who should determine the maker?"

Dispenser of
Medicine

Clifton J. Latiolais
President
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Association



Maker of
Medicine

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Association



"Too many doctors are indifferent to the economic consequences of their decisions." So stated a recent issue of *Medical News Report* (December 4, 1972), an independent weekly newsletter published by former AMA Chief Executive F. J. L. Blasingame, M.D.

Doctor, are you indifferent...?

In discussing an anticipated increase in Blue Shield rates, Dr. Blasingame's newsletter had this to say:

"In general, it can be said, MD's have given the impression they are not particularly concerned with the increase in cost of health care to their patients..."

"True, an MD's training is primarily scientific, but in the real world of practice, all of his scientific decisions have a price tag, or an economic impact. The economics of health care beckon the practitioner's attention. Concern for economics of medicine

When the pharmacist recommends that a drug product other than the one ordered be dispensed, the prescriber invariably permits the change when he feels the best interests of the patient will be served.

Shortcomings of Pro-Substitution Argument

The fact remains that it is necessary for the prescriber to know that the change is being contemplated, and to be in a position to consent or demur. Without that opportunity, the unilateral decision of the pharmacist, made in the absence of clinical knowledge of the patient, could expose him to needless risks, and in addition, jeopardize the relationship between the professions of Pharmacy and Medicine. In my view, there is nothing in the pro-substitution argument that offsets these risks.

The Issue of Drug Knowledge

Substitution advocates claim that the primary justification for changing the rules is the desire to better utilize pharmacists' knowledge about drugs. Yet the pharmacist's task to keep current on the entire field of drug therapy, to some degree, puts him at a disadvantage. Most often, a practicing physician will need expert knowledge of no more than 25

CENTRO MEDICO DE MAYAGUEZ – PASADO, PRESENTE Y FUTURO

Gilberto Cardona, MD, FAAP

Es la intención de este artículo servir de marco de referencia a los trabajos que aparecen en este número del Boletín. Por tal razón repaso a continuación el pasado, presente y futuro de la institución.

Pasado

Surgió la idea de la construcción de este complejo hospitalario en el año 1960, y el Alcalde actual de la ciudad de Mayagüez, entonces Representante a la Cámara, Honorable Benjamín Cole, presentó el proyecto de ley que creó el Centro Médico de Mayagüez el día 9 de marzo de 1960. Se convirtió en Ley el día 11 de junio del mismo año. Para esa época servía de hospital base a la región el Hospital de Distrito de Aguadilla. Existían un gran número de problemas y estrecheces que impedía una práctica buena de la medicina, razón por la cual se agravaba la situación vigente.

Casi al final de la construcción de las estructuras físicas del nuevo hospital, (1966-68) se inició en el viejo Hospital de Distrito de Aguadilla una corriente de superación profesional que marcaría el inicio del concepto actual de trabajo que permea hoy al Centro Médico de Mayagüez. Distinguidos profesionales en el campo de la salud y un gran número de técnicos auxiliares aunaron sus ideas y esfuerzos para desarrollar y mantener el concepto profesional que ahora vemos en el Centro Médico de Mayagüez. Surgió pues, en mi opinión, el concepto profesional del Centro Médico de Mayagüez en el Hospital de Distrito de Aguadilla. Fue allí que se obtuvo el reconocimiento por el Consejo de Educación de la Asociación Médica Americana para los primeros departamentos reconocidos del Centro Médico de Mayagüez, primero el Departamento de Pediatría, seguido por el Departamento de Maternidad.

Ya aquí el pasado y el presente comienzan a fundirse en uno solo.

Presente

Forman parte del Centro Médico de Mayagüez las siguientes facilidades: Centro de Rehabilitación, Hospital de Salud Mental, Casa de Salud de 200 camas, Residencia para Médicos y Enfermeras y Hospital Ramón Emeterio Betances (la facilidad clínica más importante del Centro Médico).

Los cuatro departamentos clínicos (Medicina, Pediatría, Maternidad y Cirugía) están aprobados por el Consejo de Educación de la Asociación Médica Americana. Sus 20 plazas de internado, tercero en importancia entre los hospitales del Gobierno de Puerto Rico, están también aprobados. Asociado a la Escuela de Medicina de Puerto Rico, el hospital ofrece un curso teórico-práctico para recién graduados. Es el único hospital en Puerto Rico que ofrece el año académico de experiencia clínica requerido por la Asociación Médica Americana a egresados de escuelas que exigen un internado pre-grado o servicio social para otorgar el grado de doctor en medicina (La "Quinta Trayectoria"). Ofrece el hospital también enseñanza a estudiantes de cuarto año de la Escuela de Medicina de Puerto Rico y estudiantes del tercero y cuarto año de universidades extranjeras. La activa labor académica, que marca el ritmo en esta facilidad hospitalaria relativamente joven, ya se reconoce entre los hospitales de enseñanza. El Hospital Ramón Emeterio Betances intenta lograr la integración de servicio y educación sin menoscabo de una u otra. El número de médicos en entrenamiento sigue creciendo (Tabla I). El servicio prestado también va en aumento (Tabla II) y para dar cohesión a ambas actividades cuenta el hospital con 48 médicos en su Facultad de enseñanza.

Debemos señalar que tiene nuestro hospital un excelente servicio de genética y endocrinología pediátrica y la sección de medicina cardiovascular está en desarrollo.

Futuro

Estamos empeñados en desarrollar más completamen-

**TABLA I: COMPARACION DE NUMERO DE ESTUDIANTES Y MEDICOS
EN ENTRENAMIENTO ENTRE 1972 Y EL 1973**

	1972	1973
Residentes	32	38
Internos	14	20
Quinta Trayectoria	1	2
Estudiantes de Medicina	0	6

TABLA II: ESTADISTICAS

	Año 1971-72	Año 1972-73
Admisiones	12238	13018
Altas	11694	12253
Días Pacientes	82672	93055
Operaciones	6232	9472
Partos	4139	3741
Exámenes de Laboratorio	2,152,570	2,346,941
Núm. de Clínicas Efectuadas	3363	3635
Núm. de Pacientes Vistos en Clínicas Externas	77818	76213
Núm. de Pacientes Vistos en Emergencia	42046	51017

te nuestros departamentos primarios y crear nuevas actividades y secciones. Sigue siendo nuestra meta un servicio de calidad y para lograrlo prepararemos mejores servidores mediante una mejor formación profesional.

En nuestra agenda está incluido el poder ofrecer estudios médicos en un futuro cercano pues nuestra facultad y facilidades nos capacitan para ello.

Just what do you get for your AMA dues?

You get a package of personal and professional services and benefits you've probably never been fully aware of.

You get insurance programs at a cost considerably lower than those purchased on an individual basis. A \$250,000 Excess Major Medical Policy. Group Life. Disability Income Insurance. Professional Liability Insurance (in co-sponsorship with your state society.) Then there's the AMA Members Retirement Fund.

You get a comprehensive medical library to help you do your research. An editing service for your articles. Information and reports on

medical and health subjects from any AMA department.

You get publications to keep you abreast of medical and health developments. *JAMA*. *American Medical News*. And *Prism*, the new socioeconomic journal.

You get the Physician's Placement Service to help you find a place to practice or locate an associate. And if you're a resident winding up your training, there's a special workshop to help prepare you for setting up your practice.

All these are just a few of a broad spectrum of benefits and services you get for your dues. But even more important, you get a strong and effective national spokesman to represent you, your interests and your views.

Join us.

We can do much more together.

American Medical Association
535 N. Dearborn St./Chicago, Ill. 60610



ROCHE announces new

BACTRIMTM

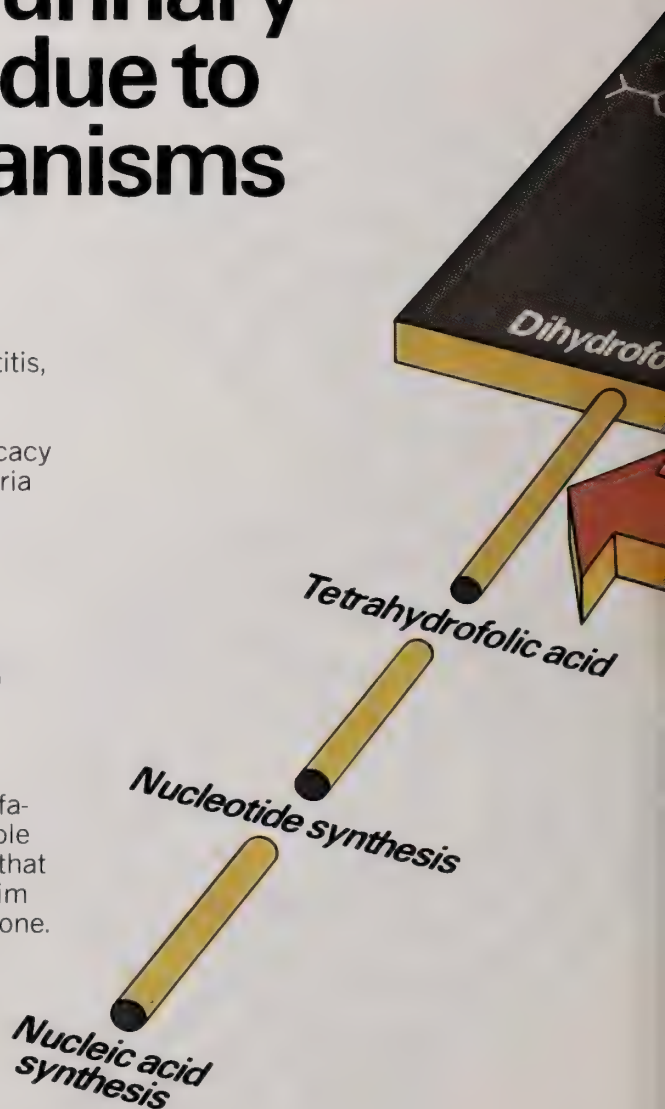
Each tablet contains 80 mg trimethoprim and 400 mg sulfamethoxazole.

a new type of antibacterial for a two-pronged attack against chronic urinary tract infections due to susceptible organisms

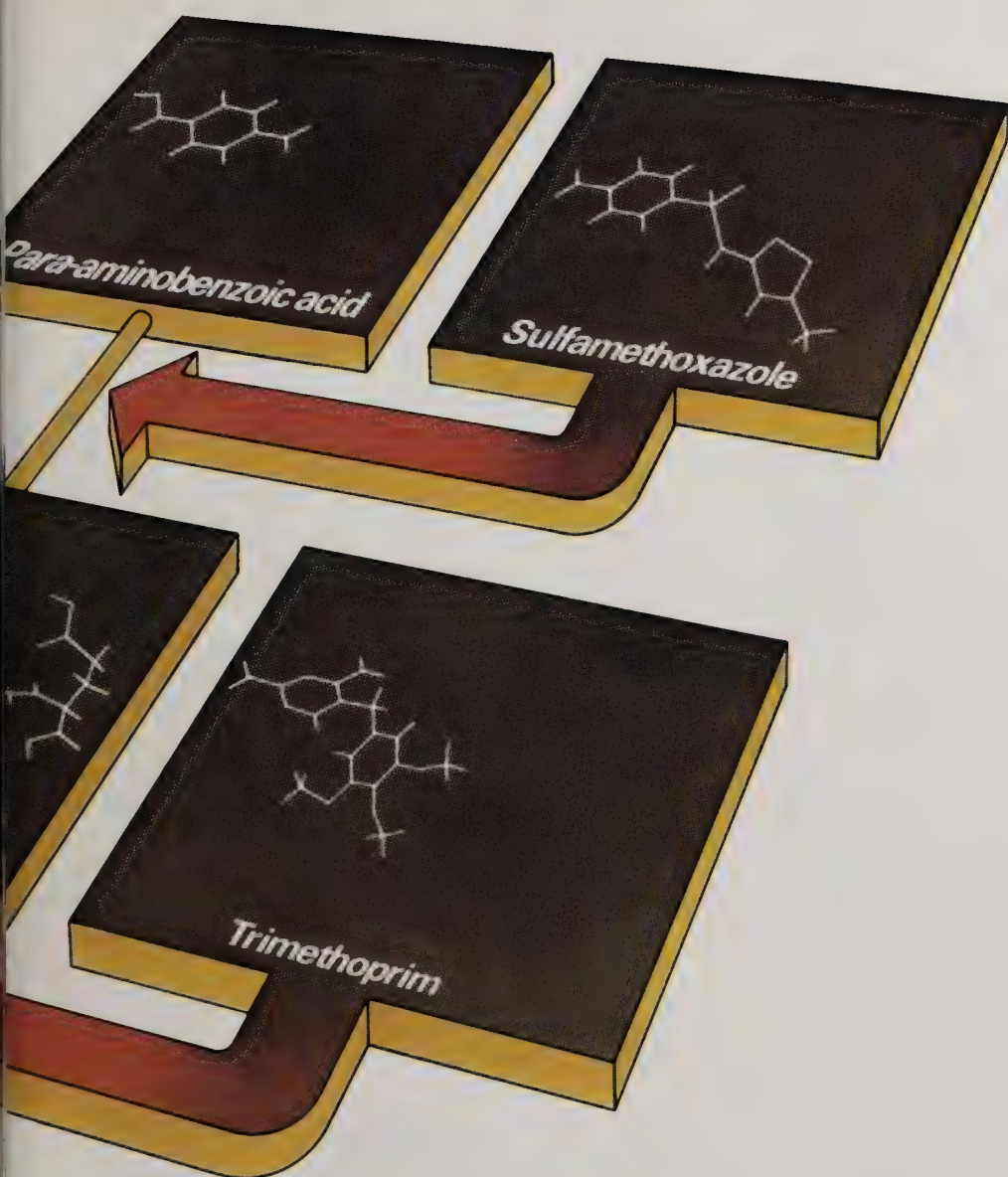
Bactrim is highly effective in the treatment of these infections – primarily pyelonephritis, pyelitis and cystitis, when due to susceptible organisms (usually *E. coli*, *Klebsiella-Enterobacter*, *Proteus mirabilis*, and, less frequently, indole-positive proteus species). This efficacy is related to the unique mode of action against bacteria (see opposite page), an action that, in effect, makes Bactrim a new type of antibacterial.

Bactrim significantly superior to constituents in patients with obstructive complications

In the presence of obstructive uropathy, Bactrim has demonstrated efficacy which is superior to either sulfamethoxazole or trimethoprim alone against susceptible organisms. In addition, *in vitro** studies have shown that bacterial resistance develops more slowly with Bactrim than with either trimethoprim or sulfamethoxazole alone.



*Please note that clinical conclusions cannot be extrapolated from *in vitro* studies.



interrupts life cycle of susceptible bacteria

Unique mode of action interrupts the life cycle at two important points, thereby impeding the production of nucleic acids and proteins essential to these bacteria. These consecutive interruptions occur because sulfamethoxazole and trimethoprim resemble naturally existing substrates. By competitive replacement of these substrates, they inhibit further synthesis.

new **BACTRIM**TM

Each tablet contains 80 mg trimethoprim and 400 mg sulfamethoxazole.

for chronic urinary tract infections

Before prescribing, please see complete product information on last page of advertisement.

Excellent clinical response in chronic urinary tract infections

A multiclinic, double-blind study* of response to a ten-day course of therapy in 471† patients with chronic urinary tract infections demonstrated the superiority of Bactrim. On the 10th day after initiation of therapy, 91.7% (of 168 patients) showed significant bacteriological response to Bactrim compared with 81.2% (of 144 patients) to trimethoprim and 64.5% (of 155 patients) to sulfamethoxazole. In patients with obstructive complications, 10th day response was 94.8% (of 97 patients) to Bactrim, 72.9% (of 85 patients) to trimethoprim and 58.5% (of 94 patients) to sulfamethoxazole.

Excellent response maintained

Bactrim proved equally impressive in maintaining this bacteriological response. In the above study, after ten-day therapy with Bactrim, 68.4% of patients with chronic urinary tract infections maintained response for up to 42 consecutive days, compared with 59.7% with trimethoprim and 44.4% with sulfamethoxazole. In patients with obstruction, 70.8% of those on Bactrim maintained response for up to 42 consecutive days, compared

with 49.4% on trimethoprim and 38.8% on sulfamethoxazole. The figures are particularly remarkable in cases with urinary obstruction—cases regarded as being notoriously difficult to treat.

To date, low incidence of significant side effects

Although Bactrim demonstrated impressive clinical results, it is important to note that the incidence of clinically significant adverse effects was low, mainly nausea and/or vomiting, rash, leukopenia, SGOT increase and creatinine increase.

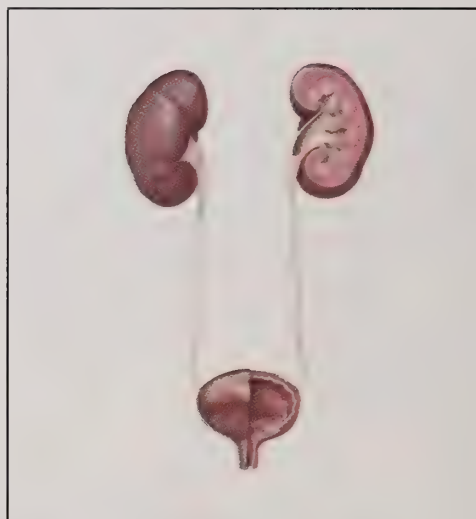
Bactrim should be given with caution to patients with impaired renal or hepatic function, possible folate deficiency and to those with severe allergy or bronchial asthma. Adequate fluid intake must be maintained. Complete blood counts, urinalyses with careful microscopic examination, and renal function tests should be performed during therapy.

Currently, the increasing frequency of resistant organisms is a limitation of the usefulness of all antibacterial agents, especially in the treatment of chronic and recurrent urinary tract infections.

Usual adult dosage: two tablets every twelve hours for 10 to 14 days; no loading dose required.

* Data on file, Hoffmann-La Roche Inc., Nutley, N.J. 07110

† 4 patients not available for evaluation at day 10.



new **BACTRIM**™

Each tablet contains 80 mg trimethoprim and 400 mg sulfamethoxazole.

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PULMONARY ALVEOLAR PROTEINOSIS — PHYSIOLOGIC OBSERVATIONS DURING AND AFTER PULMONARY LAVAGE

José Ramírez Rivera, MD, FACP *

Gerald Halprin, MD **

Clinical and experimental observations have demonstrated that the manifestations of alveolar proteinosis are, at least in part, the result of a defect in alveolar cleansing (1, 2, 3). This concept has led to the successful use of unilateral bronchopulmonary lavage, as a method of treatment (4, 5, 6, 7). In two bedridden children, ages three and four, simultaneous bilateral lung lavage has been accomplished successfully using partial cardiopulmonary bypass (8).

Concerns about hypoxemia and fear of possible complications keep many from subjecting their patients to this essential therapeutic procedure (9, 10, 11). Hospitalization is prolonged, physical incapacity maintained and unnecessary deaths continue to occur from respiratory failure (10, 11).

Pulmonary lavage is not considered more readily, perhaps, because the physiologic events occurring when one lung is filled and emptied with saline and the other lung is ventilated with oxygen are not widely known. Serial measurements of arterial blood gases during nine lavages in cases of alveolar proteinosis have documented these events and demonstrate the safety of this simple procedure (5, 12). Similar measurements in patients with asthma and bronchitis, lavaged while carefully controlling ventilation, corroborate these observations (13).

This report documents the effective control of hypoxemia which is possible during and after massive pulmonary lavage in a case of alveolar proteinosis. It also shows the rapid resolution of pulmonary infiltrates and prompt improvement in respiratory function frequently observed after lavage in this disorder.

Case Report

A 41-year old mechanical engineer was referred for pul-

From the Medical Service of the Veterans Administration Hospital, the Departments of Medicine Duke University Medical Center, Durham, North Carolina and the Mayagüez Medical Center, Mayagüez, Puerto Rico.

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** - Fellow in Pulmonary Disease, Duke University Medical Center.

monary lavage on July 9, 1971, because of breathlessness and an arterial oxygen tension (P_{O_2}) of 45 mmHg. The previous year, while working in a supervisory capacity, he had been exposed for at least one hour a day to welding fumes of ferrous metals including nickel and chromium. There was no other exposure to chemical inhalants. He was a heavy social drinker. Exertional dyspnea developed one year ago. A chest film in April 1971, showed extensive bilateral exudative infiltrates. Pulmonary tissue obtained by left thoracotomy on May 5, 1971, demonstrated alveolar proteinosis. One month after the thoracotomy, the patient returned to work but remained severely limited by exertional dyspnea.

On admission he looked vigorous and healthy. His lungs were clear, except for patchy areas of increased breath sounds at the left base posteriorly. A firm and painless liver edge was palpable 3.5 cm below the right costal margin. Radiography revealed diffuse bilateral mottled opacities radiating from the lung hili and more concentrated at the bases (Figure 1).

The serum cholesterol was 420 mg percent. His serum lactic acid dehydrogenase was 400 units (normal 90-194 units), the creatinine phosphokinase was 700 units (normal 22-180 units) the serum glutamic oxaloacetic transaminase was 100 units (normal 18-58 units).

His total lung capacity was 59 percent of the predicted normal. The low arterial oxygen tensions at rest became further depressed by exercise (Table I).

On July 13, 1971, a right pulmonary lavage was performed. The right lung was filled and emptied repeatedly with buffered saline until the effluent, which looked initially like a suspension of heavy cream, became only slightly opalescent. The lung was irrigated with 16,350 ml of saline and a volume of 16,700 ml of effluent was obtained.

As in previous cases, the arterial oxygen tensions were well maintained during the lavage. The severe, but not life-threatening, hypoxemia during the first three hours after the lavage was brought to tolerable physiologic limits by administering 100 percent oxygen by mask (Table II). On July 15 the left lung was similarly lavaged with 15,350 ml and 16,000 ml of effluent containing large amounts of sediment was obtained. Three hours after the lavage, the fraction of inspired oxygen was reduced to 40 percent and the patient was asked to sit on a chair. Five hours after the procedure oxygen therapy was stopped, the arterial canula removed from the arm and the patient was fully ambulated.

An impressive resolution of pulmonary infiltrates was noted 6 hours after the lavage of the right lung (Figure 2) and 24 hours after lavage of the left lung (Figure 3). The total and residual lung capacities increased slightly; oxygen tensions at rest and exercise were much improved (Table I). The alveolar-arterial (A-a) gradient both at rest and while breathing 100 percent oxygen decreased by 50 percent. Serum enzymes remained



Fig. 1: Chest film dated July 12, 1971 showing bilateral mottled infiltrates radiating from the hili.

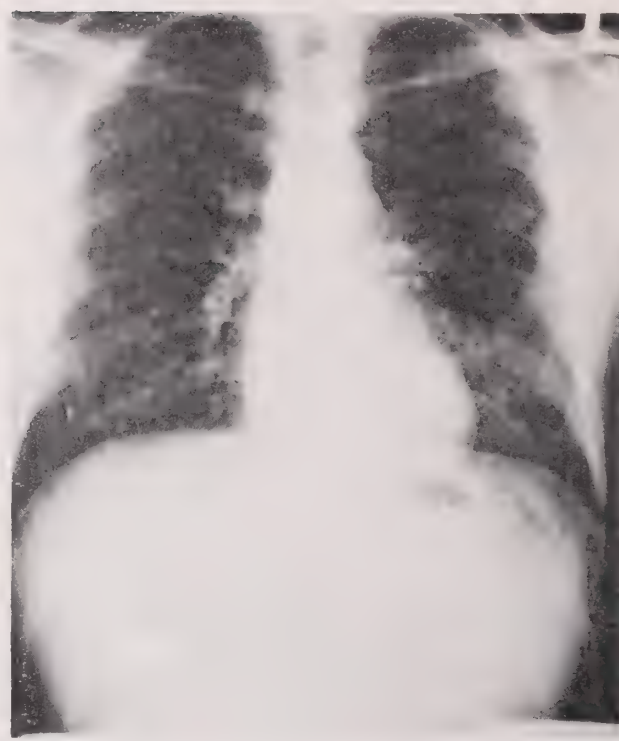


Fig. 3: Chest film dated July 16, 1971, twenty four (24) hours after lavage of left lung, showing extensive resolution of pulmonary on the left and complete resolution on the right.



Fig. 2: Chest film dated July 13, 1971, six (6) hours after lavage of right lung, showing partial resolution of right pulmonary infiltrates.

elevated. A liver biopsy on July 20 revealed fatty metamorphosis. The patient was discharged with advice to have a chest film every three months for one year and, if remission persisted, once a year thereafter.

The patient requested another pulmonary lavage and was admitted on February 26, 1973, to the Mayagüez Medical Center. His exercise tolerance had decreased. This interfered with his profession as an engineer and with sports.

On admission the lungs were clear. The painless liver edge persisted 3.5 cm below the right costal margin. The admission chest film showed little change in the residual pulmonary infiltrates on the left base when compared with the film obtained on July 16, 1971. The vital capacity was slightly increased but the oxygen tension at rest was 14 mm Hg lower than when discharged 19 months previously (Table I).

On March 1st. the left lung was lavaged with 1,250 of ml saline, 625 ml of milky fluid was obtained. No monitoring of blood gases was considered necessary. A slight liquid leak into the other lung developed with increasing pressure, therefore the procedure was terminated prematurely. The patient was not reintubated for further lavage because an important improvement was expected even with this relatively small washing. The patient was fully ambulatory five hours after the procedure. He left early the next morning to spend three days resting and swimming at a beach resort nearby. Four days after the procedure, he returned for study very happy with his increase in exercise tolerance.

Chest films after lavage showed questionable clearing. The

TABLE I: STUDIES OF RESPIRATORY FUNCTION BEFORE AND AFTER LAVAGE

	Predicted Normal	1971		1973	
		JULY 12 1 Day Before First Lavage	JULY 19 4 Days After Second Lavage	FEBRUARY 28 2 Days Before Lavage	MARCH 5 4 Days After Lavage
V. C. (L)	4.05	3.29	3.33	3.50	3.40
F. E. V. 1.0/ V. C. (Percent)	84	84	82	87	92
T. L. C. (L)	6.0	3.95	4.36	—	—
R. V. (L)	2.0	0.82	1.01	—	—
PaCO ₂ (mmHg)					
Rest	85-95	28	33.5	35	35.5
Exercise*	85-95	30	30.5	—	—
100 percent O ₂ (rest)		30.5	31	—	—
PaO ₂ (mmHg)					
Rest	85-95	56	73	59	87
Exercise*	85-95	46	59	—	—
100 percent O ₂ (rest)		341	550	—	—
(A-a) DO ₂ (mmHg)					
Rest	85-95	68	37	—	—
Exercise*	85-95	78	53	—	—
100 percent O ₂ (rest)		335	117	—	—

* 1.5 mph on a 10 percent grade

TABLE II: ARTERIAL BLOOD GASES DURING LAVAGE

	RIGHT LUNG (7/13/71)		LEFT LUNG (7/15/71)	
	PaO ₂ * mmHg	PaCO ₂ * mmHg	PaO ₂ * mmHg	PaCO ₂ * mmHg
After Intubation	229	22.5	—	—
Lung Filled	130	28	81	30
Lung Empty	57	37	73	36
End of Lavage	55	39.5	94	37

* Ventilated with 100 percent O₂

TABLE III: EFFECT OF OXYGEN BREATHING AFTER LAVAGE ON ARTERIAL BLOOD CASES

After Lavage	RIGHT LUNG (7/13/71)				LEFT LUNG (7/15/71)			
	PaO ₂ mmHg		PaCO ₂ mmHg		PaO ₂ mmHg		PaCO ₂ mmHg	
	Air	O ₂ *	Air	O ₂ *	Air	O ₂ *	Air	O ₂ *
One Hour	42	56	35	37	54	64	31	32
Two Hours	43	57	32	34	51	107	29	30
Three Hours	46	78	29.5	36	42	118	29.5	33.5
Four Hours	51	74	29	30	53	88	30.5	34.5
Five Hours	58	—	27.5	—	50	87	31	31.5
Six Hours	60	123	28	27	65	123	31.5	34

* 100 percent O₂ by face mask at 8L/min/15 min.

oxygen tensions and oxygen saturation had reached normal limits with the same ventilation (Table I). The patient was advised to seek re-evaluation by his private physician in Philadelphia in six months.

Discussion

Blood gas measurements made during the first two lavages were similar to those previously observed in patients with alveolar proteinosis (5, 12) and in asthma and bronchitis (13). Physiologically tolerable oxygen tensions were maintained during the procedure; oxygen tensions were much lower when the lung was empty than when it was full. By emptying the lungs less completely, higher oxygen tensions during the emptying phase were observed. Emptying under a slight positive pressure further minimized shunting (13). Although hypoxemia was most severe in the first three hours post lavage, it was never life-threatening. Adequate correction was obtained by administering 100 percent oxygen.

When there is extensive accumulation of alveolar material, a single lavage of each lung may not be sufficient and roentgenographic improvement may not be clearly apparent until after one or two weeks. If the oxygen saturation has not reached a satisfactory level in three or four days after the second lavage, the procedure may be repeated.

No matter how severe the hypoxemia, if the patient with alveolar proteinosis does not retain carbon dioxide, pulmonary lavage may be considered. There is very little pulmonary artery blood flow through the treated lung during the washing process. The pulmonary arteriovenous shunts resulting from persistent capillary perfusion of alveoli filled with lipoproteinaceous material will be reduced by filling the lung with liquid. Consequently, when the pulmonary involvement is extensive, there will be less hypoxemia when one lung is filled with liquid and the other lung ventilated with 100 percent oxygen than when this type of patient receives oxygen by mask or nasal catheter.

The primary cause of alveolar proteinosis remains unknown.

The failure of pulmonary alveolar clearance may be severe and continuing, or the disorder may become apparent only because the cleansing mechanism, although operative, cannot cope with previously accumulated material. Some patients may need a lung washing as early as six weeks after treatment; others may need treatment after some months or years. Those with a cleansing mechanism fully restored may not require it again. It should be emphasized that in this case, lavage was undertaken 19 months after first instituted, not because infiltrates had become much more extensive or the hypoxemia was severe, but to

improve the quality of the patient's life. This young aggressive engineer had lost some of the exercise tolerance he had regained after his initial lung washing, moderate hypoxemia interfered too much with the active life he preferred.

Asymptomatic patients with alveolar proteinosis do not need treatment. Pulmonary infiltrates can resolve spontaneously over a period of months. Resolution of pulmonary infiltrates sometimes occurs without systemic symptoms; with some frequency it is associated with pulmonary infection. Fungal infections are common causes of death. In the occasional patient who has sputum, saline and mucolytic aerosols may help debridement (endogenous bronchial flooding). In those who do not have bronchorrhea mucolytic aerosol therapy has failed (7). When pulmonary infiltrates are extensive, mucolytic aerosols may be hazardous. Massive mobilization of broncho-alveolar material may block airways and precipitate respiratory failure (10, 11). For most patients with alveolar proteinosis, pulmonary lavage is the more effective and safe method of treatment. For other patients it is the only method which is effective.

Summary

A case of alveolar proteinosis treated with pulmonary lavage is reported. Serial arterial oxygen and carbon dioxide tensions during two pulmonary lavages and in the six hours after the procedure show an effective control of ventilation and hypoxemia. The therapeutic efficacy of pulmonary lavage in the treatment of alveolar proteinosis is demonstrated and discussed.

Resumen

Se informa un caso de proteinosis alveolar tratado con lavado pulmonar. Medidas seriadas de tensiones de oxígeno y bióxido de carbono en la sangre arterial

durante dos lavados pulmonares y en las seis horas subsiguientes demuestran control efectivo de la ventilación y de la hipoxemia. La efectividad terapéutica del lavado pulmonar es demostrado y discutido.

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HIPOTIROIDISMO Y DESARROLLO SEXUAL TEMPRANO — INFORME DE UN CASO

Adolfo Pérez Comas, MD

El hipotiroidismo en la niñez se caracteriza por retraso en el desarrollo sexual, entre otras cosas. El desarrollo sexual precoz asociado a hipotiroidismo es raro. El primer caso reportado fue el de Kendle, en Inglaterra, en 1905 (1). Hasta el momento, se han reportado 23 casos en la literatura (1-16), predominando en hembras.

Recientemente evaluamos una joven con hallazgos compatibles con hipotiroidismo primario adquirido y desarrollo sexual temprano.

Reporte del Caso

M. L. M. (CMM 043549), joven de 12 años de edad al ser evaluada, fue referida debido a estatura corta. Su historial reveló retardo en el desarrollo somático, retraimiento, somnolencia, anorexia con ganancia de peso y estreñimiento de evolución progresiva desde los cuatro años de edad. A los 9 1/2 de edad presentó su menarquía, la cual fue seguida con reglas de forma anárquica, presentándose éstas hasta dos veces por mes o faltando algún mes. A los 10 años de edad comenzó a presentar desarrollo mamario y a los 11 1/2 vello púbico.

El examen físico mostró a una niña hipoactiva, con retraso en el desarrollo somático, obesidad, voz ronca, desarrollo mamario en etapa de Tanner 3 (18), vello púbico en etapa de Tanner 2, piel áspera y fría, además de bradicardia y tonos cardíacos apagados. Una estatura de 46 pulgadas con una edad-talla de 6 años y un peso de 68 lbs. con una edad-peso de 8 3/4 años (Fig. 1, Tabla I).

La radiografía torácica demostró cardiomegalia leve. La edad ósea, siguiendo a Wilkins (11) fue de 8 años, demostrando, además, disgenesia epifisaria. En la radiografía de cráneo se observó agrandamiento de la silla turca. El electrocardiograma mostró bradicardia, bajo voltaje, y acortamiento del complejo QRS.

La captación de radioyodo fue de 5 por ciento a las 24 horas, no observándose respuesta a la estimulación con TSH. Los niveles de T-3, T-4 y 17 hidrocorticoides urinarios fueron bajos. El colesterol sérico, el calcio sérico y las 17 cetosteroides urinarios fueron normales. Los estrógenos urinarios totales, al igual que el extendido vaginal fueron compatibles con el período puberal (Tabla II).



Fig. 1: Evaluación inicial.

Tras su evaluación de base, la niña fue comenzada en tiroglobulina gr. 1/4, el cual fue incrementado progresivamente hasta gr. 2 1/2. Ocho meses después de comenzar el tratamiento su peso disminuyó en 12 libras y creció 3 3/4 pulgadas, el estreñimiento y la somnolencia desaparecieron, y luce más activa (Fig. 2). Un mes después de comenzada la terapia desaparecieron las reglas, las cuales no se han vuelto a repetir. Sin embargo, el vello púbico ha aumentado, el desarrollo mamario persiste en la misma etapa y comienza a presentar vello axilar.

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TABLA I: EXAMEN FISICO ANTES DE TRATAMIENTO

DATOS GENERALES		DATOS ESPECIFICOS	
Edad Cronológica :	12 4/12 años	Desarrollo Mamario:	Tanner No. 3
Estatura:	46 pulgadas	Vello Púbico:	Tanner No. 2
Edad-Talla :	6 años	Vello Axilar:	Ausente
Peso:	68 lbs.	Galactorrea:	Ausente
Edad-Peso:	8 3/4 años	Utero:	Agrandado
S.S./S.I. *:	1.2	Mucosa Vaginal:	Efecto Estrogénico Moderado
Pulso:	52	Piel:	Aspera, Fría
Tensión Arterial:	80/50	Tonos Cardíacos:	Apagados
Voz:	Ronca	Tiroides:	Palpable Tamaño Normal, Blanda

* S.S./S.I.: Cociente segmento superior, segmento inferior.

TABLA II: EVALUACION DE LABORATORIO ANTES DE TRATAMIENTO

Edad Osea:	8 años
Radiografía de Cráneo:	Silla Turca Agrandada
Radiografía Torácica:	Cardiomegalia leve
Captación Radioiodo (24 hrs.):	5 por ciento (Normal 10-35 por ciento)
Estimulación TSH:	2.5 por ciento de Captación
T-4 (Radioensayo):	Ougn. T-4 I por ciento (Normal: 2.6-7.2)
T-3 (Radioensayo):	20 por ciento (Normal: 25-35 por ciento)
Colesterol Sérico:	215 mg por ciento
Calcio Sérico:	10.1 mg por ciento
Estrógenos Totales Urinarios:	15.73 ugn/24 hrs.
17 Hidroxicorticosteroides Urinarios:	1.42 mg/24 hrs.
17 Cetosteroides Urinarios	4.39 mg/24 hrs.

Nota: Los niveles de FSH, TSH, LH y Anticuerpos a tiroides no fueron realizados por carecer de facilidades.

Su edad ósea, 8 meses después de comenzada la terapia, es de 12 años. Su edad talla es de 7 años 4 meses, aproximadamente.

Discusión

El desarrollo sexual en un niño hipotiroideo suele ser retrasado. En la literatura mundial se han reportado, sin incluir nuestro caso, 23 niños con hipotiroidismo y desarrollo sexual temprano, de los cuales 18 son hembras y 5 son varones (16). En 19 de ellos el desarrollo sexual regresó tras la terapia, en 3 progresó o

se mantuvo estable y en uno (1) no hay datos. Entre los casos reportados hay 4 sujetos que además presentaban síndrome de Down. La asociación de hipotiroidismo y síndrome de Down es, también, extremadamente rara, habiéndose reportado hasta el presente 16 casos (17).

Nuestra paciente presentó los caracteres de hipotiroidismo primario adquirido. La menarquía temprana y las reglas anárquicas desaparecieron al iniciar la terapia sustitutiva con tiroglobulina. Más adelante tuvo



Fig. 2: Ocho meses después de comenzada la terapia.

desarrollo de caracteres sexuales secundarios, a una edad compatible con una hembra normal. El comienzo de la menarquía a los 9 1/2 años resulta algo temprano, a pesar de que otros caracteres sexuales secundarios pueden comenzar a aparecer entre los 8 y 9 años (18, 19). Resulta, además, atípico, presentar menarquía como primera manifestación de desarrollo sexual, en lugar de presentar desarrollo mamario (telarquía) o vello púbico (pubarquía). El hecho de que desaparezcan las reglas, al instaurarse la terapia, confirma, de modo indirecto, que estas eran secundarias a la enfermedad tiroidea subyacente.

La edad ósea no corresponde a la esperada para una menarquía, pero sí a la de un hipotiroidismo. La disgenesia epifisaria en centros de osificación posteriores a los 4 años sugieren que de esta niña no haber

presentado desarrollo sexual, la edad ósea habría sido más baja. Entre los casos reportados en la literatura, 15 presentaron retardo en la edad ósea (5, 7-16), 6 eran normales (2, 4-6, 10, 16) y en 2 no hay datos (1, 3). En los casos con retardación de maduración ósea, el promedio de retraso es de 3.64 años.

El agrandamiento de la silla turca sugiere una hiperplasia de la hipófisis, que podría tener relación con el desarrollo sexual precoz. Entre los casos reportados, 11 presentaron agrandamiento de la silla (2, 5, 6, 8, 12, 13, 15-16), 9 no presentaron agrandamiento (7, 9-11, 14-16) y en 3 no hay datos (1, 3-4); observándose, agrandamiento de la silla turca en el 55 por ciento de los casos para los cuales hay datos.

Dieciseis casos reportados presentaron con tejido mamario (3, 4-6, 8-11, 13-14, 16), en 2 estaba ausente (4, 12), y en 5 no hay datos (7, 15). El vello púbico estaba presente en 9 casos (1, 5, 8, 10, 13, 15-16), y ausente en 14 casos (2-7, 9-12, 14-16). Diecisiete pacientes mostraron sangría vaginal (1-14, 16), 1 no la tuvo (10), y en 4 no hay datos (15). De los 23 casos, sólo en 3 se observó un regreso del desarrollo sexual al ser tratados (15).

La función glucocorticoide adrenal baja, ha sido reportada previamente en otros casos de hipotiroidismo (11). Su causa no está bien definida.

Con nuestro caso, son 24 los pacientes afectados de este síndrome que han sido reportados, pero sospechamos que existen aún más, los cuales no han sido reportados por falta de una evaluación completa. En nuestro caso, tenemos la sospecha que su hipotiroidismo primario adquirido es secundario a tiroiditis linfocitaria crónica, debido a los caracteres de su glándula tiroidea y a la alta incidencia de la condición en Puerto Rico.

La causa del desarrollo sexual precoz en pacientes hipotiroideos no es bien conocida. Recientemente, Costin y colaboradores reportaron 2 pacientes en los cuales se determinaron niveles de hormona tireotropa (TSH), hormona luteinizante (LH), hormona foliculoestimulante (FSH) y prolactina, las cuales estaban elevadas (16). Tras la terapia sustitutiva con tiroides sus valores disminuyeron a los niveles normales. Ellos han propuesto que al disminuir las hormonas tiroideas circulantes, la hipófisis y el hipotálamo se hacen hiperfuncionantes para estimular la tiroides defectuosa. Asociado a ello aumenta la secreción de otras hormonas hipofisarias dando lugar, en estos casos, a desarrollo sexual precoz (5, 16).

Resumen

El hipotiroidismo asociado a desarrollo sexual tem-

prano es una condición rara, representando la excepción en los casos de hipotiroidismo. Hasta el momento, incluyendo nuestro caso, se han reportado 24 casos en la literatura mundial. En su patogenia se sospecha un desbalance en los servomecanismos de regulación hipotálamo-hipofisario inducido por la carencia de hormonas tiroideas circulantes.

Summary

Hypothyroidism associated with early sexual development is a rare entity. This paper concerns the 24th case reported in the literature.

A 9 1/2 year old female presented with growth retardation, anorexia, weight gain, constipation, somnolence, dullness and menarche at 9 1/2 years old without other evidence of sexual maturation. Anarchic menses and breast development started at 10 years of age and pubic hair development at 11 1/2 years. Laboratory studies suggested acquired primary hypothyroidism. After treatment with Proloid for 8 months, the menses disappeared but the sexual development persisted and increased slightly.

Agradecimiento

Agradecemos a los Dres. Miguel A. Lasalle y Pedro L. Valle la evaluación inicial del caso, y al Dr. Héctor L. Rodríguez Fernández, la revisión y crítica del manuscrito.

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¿POR QUE UN CURSO TEORICO-PRACTICO PARA GRADUADOS EN EL EXTRANJERO?

Alejandro Jiménez Méndez, MD

*Ahora vemos por espejo, oscuramente;
mas entonces veremos cara a cara.....
Ahora conozco en parte; pero entonces
conoceré como fui conocido. Corintios 1:12*

Toda nueva experiencia puede tornarse frustrante si uno carece de las armas necesarias para enfrentarse a las situaciones que engendran estas experiencias. La práctica de la medicina constituye una de ellas y el ejercicio de la misma, será placentero cuando logramos integrar en un solo hecho, conocimientos, destrezas y amor.

Cerca de treinta por ciento de los que ejercemos en Puerto Rico, procedemos de las aulas españolas (1). Con gran esfuerzo, y tras varios años de estudio, regresamos a nuestra Isla con un caudal de conocimientos que nos habilita para la comprensión de la literatura médica o para entendernos con nuestros experimentados colegas. Pero carecemos de la práctica necesaria para aplicar estos conocimientos.

El año obligatorio de internado continúa siendo uno de los recios pilares en nuestra formación profesional, pues constituye una experiencia única, en la cual de la noche a la mañana, sin más, el estudiante de aulas deja de ser estudiante para despertar en el ejercicio pleno de sus responsabilidades como médico. Es en este año de internado donde mayormente se adquieren destrezas en el ejercicio de la medicina y donde se estructura una de las piezas fundamentales de la medicina actual: el médico generalista.

Me pregunto: ¿por qué motivos el año de internado es recordado por muchos médicos graduados en el extranjero como uno de grandes vicisitudes, difícil y lleno de escollos? Conocí a uno de ellos que vivió días de intensa angustia durante su internado con temor a su próxima guardia, al reconocer su incapacidad, su perplejidad e indecisión ante el enfermo. Sufría intensa

ansiedad en las noches cuando recaía sobre él *toda* responsabilidad en el manejo del paciente. La contestación, vertida ya anteriormente, radica en la práctica forzada de la medicina cuando aún no se han integrado en él los elementos del trínomio: conocimientos, destrezas y amor. Y así, el año de internado, que pudo haber sido una experiencia agradable, de gran aprendizaje, se convierte en una situación embarazosa, poco edificante y a veces frustrante y deformante. Sin duda esta experiencia malsana se manifestará en la práctica de una medicina de mediana calidad.

El Curso Teórico-Práctico que ofrece la Escuela de Medicina de Puerto Rico, en el Centro Médico de Mayagüez, constituye, en mi propia experiencia y quizás sin la intención de los señores que lo concibieron, el único intento real de aproximar los fundamentos que facultan al médico para el ejercicio de su arte y de su ciencia. En este curso, a través de seis meses, me he integrado a la medicina en una forma amena, gradual y progresiva. Los conocimientos, destrezas y amor hacia el prójimo y la profesión, se fueron imbricando paulativamente dándole sentido y complacencia a mis funciones como médico. De una manera acelerada recorrí por los campos de la Anatomía, la Fisiología, Psiquiatría, Dermatología, Hematología, Bacteriología, Higiene, Medicina, etc. También tuve la oportunidad de practicar la toma de datos mediante historiales y exámenes físicos, paracentesis, toracentesis, punciones lumbares, venoclisis, legrados, lavados gástricos y otros. Finalmente, tuve la oportunidad de familiarizarme sistemáticamente con el funcionamiento de un gran Centro Médico, conocer sus dependencias, sus servicios, sus facilidades y sus limitaciones y he podido relacionarme íntimamente con personal y enfermos del hospital y desenvolverme en circunstancias que infunden nobles sentimientos. El Curso Teórico-Práctico me ofreció muchísimas ventajas: conferencias dictadas por celebridades de la medicina puertorriqueña, películas, discusión de casos clínicos, manejo de pacientes, horas de estudio. Dispuse de más tiempo libre que el que se ofrece en el internado, lo que no deja de ser una condición favorable para estudiar para los exámenes de reválida, que dicho sea de paso,

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en su esencia, el curso preponderará hacia ese fin.

Desde aquí invito a mis incipientes compañeros de profesión, especialmente a los graduados en el extranjero, a que tomen en consideración las ventajas del Curso. Este curso les habilitará para el examen de reválida y mejor aún, les ofrecerá la oportunidad de integrarse como médicos, lo que redundará en un mejor desenvolvimiento durante el año de internado y un

recuento feliz de una etapa única en la vida.

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EL SUBEXTERNADO: EXPERIENCIA CLINICA DE LA PREMEDICA

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Harry Agis ****

Por largos años los premédicos de Puerto Rico se quejan de lo árido que resultan los estudios universitarios, del limitado estímulo filosófico y orientador que se ofrece al que quiere ser médico. Si es cierto que la premédica es una fase formativa para el estudiante no es menos cierto que estudiantes originalmente bien motivados, flaquean en sus esfuerzos porque la premédica les resulta "alejada" de la carrera que ellos ambicionan.

Hace dos años un pequeño grupo de estudiantes de premédica visitaron la "guardia" del Director de Educación Médica. Su petición para ver operaciones fue denegada. Aceptamos que el estudiante que tiene verdadera vocación para ser médico sería beneficiado si dejara semanalmente, aunque fuera por pocas horas la tediosa rutina universitaria y tuviera un contacto aplicado con la medicina.

Con este propósito organizamos, con la ayuda del departamento de enfermería y el Programa de Asistencia Médica del Centro Médico de Mayagüez, una experiencia voluntaria al comienzo del año académico 1971-72 para estudiantes de premédica.

A continuación presentamos los objetivos de esta orientación y las observaciones hechas durante el último año.

Materiales y Métodos

Todos los estudiantes de tercer y cuarto año de bachillerato en Ciencias, miembros del Círculo de Premédicos del Colegio Agricultura y Artes Mecánicas fueron elegibles para la experiencia. Los interesados obtuvieron los siguientes materiales:

1. Tarjeta identificación
2. Batas distintivas
3. Plástico con su nombre

Las horas de asistencia se contabilizaron de la misma forma

que otros voluntarios. Se ofreció una orientación inicial de seis semanas (Tabla I); ésta fue seguida por una rotación de dos semanas por cada departamento (Tabla II). Se obtuvo una reacción subjetiva del grupo al final del entrenamiento. Después de la rotación inicial los que así lo interesaban continuaron de voluntarios donde les fue más atractivo.

Observaciones

De los 60 estudiantes elegibles para el entrenamiento clínico voluntario, 15 participaron activamente. Contabilizamos un total de 447 horas de servicio con un promedio de 29 horas por estudiante.

Aproximadamente un 50 por ciento de las horas no fueron registradas en las hojas de asistencia por estas no estar disponibles durante las horas cuando el estudiante sirvió como voluntario.

Los estudiantes sirvieron por lo general por la noche y durante los fines de semana. Hubo una tendencia a quedarse más de dos semanas en la rotación asignada buscando una identificación más completa en el primer servicio asignado. Emergencia fue el servicio preferido. Esta actividad educativa frecuentemente suplantó otras actividades extracurriculares típicas de estudiantes universitarios.

Los jóvenes premédicos asimilaron con gran facilidad el funcionamiento de los diversos profesionales en el ambiente hospitalario. Se ubicaron en la institución no solo en busca de aprender sino también con fines de servir.

El premédico comprendió la importancia de la privacidad del historial clínico y aprendió a relacionarse con el paciente como enfermo y como ser humano.

Conclusiones

El subexternado relaciona exitosamente al estudiante interesado con el funcionamiento de un hospital.

La experiencia más valiosa es la de conocer al humano como paciente y la de entender sus inquietudes y padecimientos. No es necesario tener un grado universitario para comprender la función social y psicológica que desempeña un médico. El estudiante de premédica puede adquirir destrezas y conocimientos

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TABLA I: ORIENTACION PRELIMINAR PARA EL SUBEXTERNADO 1972-73

-
- I- ENFERMERIA
a) Filosofía b) Propósitos c) Objetivos d) Normas del Servicio
Por: Carmen Atresino, B.S. R.N., Directora Servicio de Enfermería
- II- EL HOSPITAL, EL MEDICO Y LA COMUNIDAD
a) Tipos de Hospitales b) Las especialidades médicas c) Relación del médico y del paciente
d) Educación e) Investigación f) El médico y la comunidad
Por: José Ramírez Ramírez, MD, Jefe, Departamento de Medicina y Director de Educación Médica e Investigaciones Clínicas, Región Oeste.
- III- ORGANIZACION DEL HOSPITAL DR. RAMON EMETERIO BETANCES
a) Filosofía b) Objetivos c) Propósitos d) Normas del Hospital
Por: Herson Morales, M.A., Administrador Auxiliar del Hospital
- IV- FUNCIONES DE LOS MIEMBROS VOLUNTARIOS
a) Descripción de Funciones b) Uniforme c) Asistencia
Por: Ivonne Ramírez de Serna, M.A., Directora del Programa de Asistencia Médica
- V- ETICA PROFESIONAL
a) Principios de Comunicación b) Reacciones Interpersonales
Por: Aida Sotomayor, M.A. R.N., Coordinadora Programa de Desarrollo de Personal
-

TABLA II: OBJETIVOS EDUCACIONALES DEL SUBEXTERNADO POR DEPARTAMENTOS

-
- I- DEPARTAMENTO DE MEDICINA
1. Aprender a relacionarse con el paciente y a redactar la parte social y personal del historial clínico.
 2. Aprender a obtener o interpretar las medidas obtenidas de:
 - a) Temperatura
 - b) Presión Arterial
 - c) Pulso
 - d) Respiración
 3. Aprender a alimentar y cambiar posición de pacientes.
 4. Aprender a tomar electrocardiogramas.
 5. Observar procedimientos.
- II- DEPARTAMENTO DE CIRUGIA
1. Aprender asepsia pre-operatoria.
 2. Aprender a conocer de manera general bandejas de instrumentos quirúrgicos.
 3. Aprender a hacer curaciones sencillas.
 4. Observar procedimientos.
- III-DEPARTAMENTO DE OBSTETRICIA Y GINECOLOGIA
1. Aprender a sacar sangre.
 2. Aprender a obtener un historial obstétrico.
 3. Aprender a relacionarse con la mujer de parto.
 4. Orientación sobre asepsia pre y post parto.
- IV-DEPARTAMENTO DE EMERGENCIA
1. Aprender a relacionarse con el accidentado y su familia.
 2. Aprender a sacar sangre.
 3. Aprender a hacer curaciones sencillas.
 4. Servicio de escolta.
- V- DEPARTAMENTO DE PEDIATRIA
1. Observación de infantes normales.
 2. Aprender a vestir, desvestir, pesar y bañar un infante.
 3. Aprender a relacionarse con un niño enfermo.
 4. Aprender a relacionarse con la madre de un niño enfermo.
 5. Aprender cómo se prepara y se administra la fórmula para bebés.
-

básicos que lo hacen útil al paciente y a la institución. El estudiante es bien recibido como ciudadano instruído ante el cuerpo médico y de enfermería.

Resumen

Se presentan los objetivos educacionales de una rotación clínica para estudiantes de premédica. Los estudiantes, voluntarios, comprendieron la función del hospital y aprendieron a relacionarse con el enfermo y sus familiares. Las destrezas aprendidas hicieron al estudiante útil al paciente y a la institución. El estudiante fue bien recibido y sus objetivos aceptados

por el personal de médicos y de enfermería.

Summary

We present the educational objectives and observations of a clinical rotation for college students in a premedical program. The students working as volunteers learned well the functions of the hospital. They learned to understand the need of the ill person and his relatives. The basic skills learned made him useful to the patient and the institution. His presence was welcomed and his objectives understood by the physicians and nursing staff.

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Men with trichomonal infection are virtually always asymptomatic, which is why they seldom know they have the disease. But many do have it, nevertheless.

Trichomonal infection is so common that estimates¹ indicate one out of every four women of reproductive age has the disease. *Almost half of the husbands of women infected with Trichomonas vaginalis have it, too.*²⁻⁹

CONCURRENT THERAPY WITH FLAGYL PROVIDES ALMOST CERTAIN CURE FOR BOTH OF THEM.

- It is the most effective drug available for the treatment of trichomoniasis in both men and women.
- In men, it eliminates infection from the genitourinary tract.
- In women, it eliminates trichomonal infection from the vagina, the paravaginal crypts, cavities, and glands.
- Consistent cure rates above 90 percent are to be expected. The rate often approaches 100 percent.
- Simple, sure treatment for women: One 250-mg. tablet three times daily for ten days.
- Simple, sure treatment for men: One 250-mg. tablet twice daily for ten days concurrent with treatment of the female partner.
- Side effects are generally mild and infrequent.
- Flagyl is economical because it is so effective.

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Indications: For the treatment of trichomoniasis in both male and female patients and in the sexual partners of patients with a recurrence of the infection provided trichomonads have been demonstrated by wet smear or culture. The oral tablets are indicated also for acute intestinal amebiasis (amebic dysentery) and amebic liver abscess.

Contraindications: Evidence or history of blood dyscrasia, active organic disease of the CNS, the first trimester of pregnancy and a history of hypersensitivity to metronidazole.

Warnings: Use with discretion during the second and third trimesters of pregnancy and restrict to those pregnant patients not cured by topical measures. Flagyl (metronidazole) is secreted in the breast milk of nursing mothers. It is not known whether this can be injurious to the newborn.

Precautions: Mild leukopenia has been reported during Flagyl treatment and, therefore,

tial leukocyte counts are recommended before and after treatment with the drug, especially if a second course is necessary. Avoid alcoholic beverages during Flagyl therapy because abdominal cramps, vomiting and flushing may occur. Discontinue Flagyl promptly if abnormal neurologic signs occur. Exacerbation of moniliasis may occur. In amebic liver abscess, aspirate pus during metronidazole therapy.

Adverse Reactions: Nausea, headache, anorexia, vomiting, diarrhea, epigastric distress, abdominal cramping, constipation, a metallic, sharp and unpleasant taste, furry or sore tongue, glossitis and stomatitis possibly associated with a sudden overgrowth of *Monilia*, exacerbation of vaginal moniliasis, an occasional reversible moderate leukopenia, dizziness, vertigo, incoordination and ataxia, numbness or paresthesia of an extremity, fleeting joint pains, confusion, irritability, depression, insomnia, mild erythematous eruptions, "metallic" taste, flushing, dizziness of the

mouth, vagina or vulva, pruritus, dysuria, cystitis, a sense of pelvic pressure, dyspareunia, fever, polyuria, incontinence, decrease of libido, nasal congestion, proctitis, pyuria and darkened urine have occurred in patients receiving the drug. Patients receiving Flagyl may experience abdominal distress, nausea, vomiting or headache if alcoholic beverages are consumed. The taste of alcoholic beverages may also be modified. Flattening of the T wave may be seen in ECG tracings.

Dosage and Administration: For Trichomoniasis. In the female: One 250-mg. tablet orally three times daily for ten days. Courses may be repeated if required in especially stubborn cases; in such patients an interval of four to six weeks between courses and total and differential leukocyte counts before, during, and after treatment are recommended. Vaginal inserts of 500 mg. are available for use, particularly in stubborn cases. *When the vaginal inserts are used one 500-mg insert is placed high*



in the vaginal vault each day for ten days and the oral dosage is reduced to two 250-mg. tablets daily during the ten-day course of treatment. Do not use the vaginal inserts as the sole form of therapy. *In the male:* Prescribe Flagyl only when trichomonads are demonstrated in the urogenital tract, one 250-mg. tablet two times daily for ten days. Flagyl should be taken by both partners over the same ten-day period when it is prescribed for the male in conjunction with the treatment of his female partner.

For Amebiasis. *Adults:* For acute intestinal amebiasis, 750 mg. orally three times daily for 5 to 10 days. For amebic liver abscess, 500 to 750 mg. orally three times daily for 5 to 10 days. *Children:* 35 to 50 mg./kg. of body weight/24 hours, divided into three doses, orally for ten days.

Dosage forms: Oral tablets 250 mg.
Vaginal inserts 500 mg.

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Dis. 36:21-26 (March) 1960. 8. Bertrand, P., and Leulier, J.: Essais cliniques sur la trichomonase des partenaires des femmes infestées (Proceedings of the 1st Canadian Symposium on Non-Gonococcal Urethritis and Human Trichomoniasis, Montreal, 1959), *Gynaecologia* 149:93-96 (Suppl.) 1960. 9. Poole-Wilson, D. S.: The Diagnosis and Management of Chronic Infection of the Bladder, *Practitioner* 186:429-437 (April) 1961.

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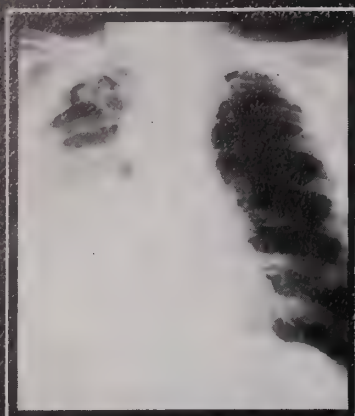
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OPERACION TIERRA ADENTRO

Luis Acevedo Lazzarini, MD

Durante el mes de mayo de 1973, diez estudiantes de medicina de la Universidad de Puerto Rico, diseñamos un proyecto de verano dirigido a pequeñas comunidades del centro de nuestra isla. Queríamos probar si los estudiantes de medicina podíamos llevar un programa de orientación y prevención de enfermedades a personas aisladas y distantes de las grandes urbes. Queríamos observar la magnitud de los problemas de salud en esta población.

Métodos

El área de Castañer, población con un magnífico hospital rodeado de pequeñas comunidades agrícolas, fue escogido como base para el proyecto. Se seleccionó para estudio el Cerrote de Las Marías, Vilella de Lares y el sector Maguelles de Maricao: tres comunidades aisladas con menos de 30 familias de población.

Se utilizó la familia como unidad de trabajo.

El grupo médico participó voluntariamente y sin remuneración o acreditación académica. Se compuso de cuatro estudiantes entrantes el próximo agosto a su primer año de estudios de medicina, tres de primer año, dos de segundo año y un médico recién graduado, divididos en tres equipos.

El proyecto duró cuatro semanas. La primera se dedicó a capacitar al equipo en técnicas de entrevista, manejo de los equipos de detección, administración de vacunas y tuberculinas, y la discusión de los posibles problemas médicos que *a priori* se habían planteado. Se dio énfasis a los métodos que se utilizarían para evaluar la labor diaria del equipo con la comunidad, para así poder modificar el diseño original, según fuera necesario. Durante la segunda semana se entrevistaron por medio de un cuestionario a las familias del área para determinar los problemas de salud de cada una de las comunidades.

En las dos semanas restantes, se trabajó directamente con las familias.

La manera de llegar mejor a nuestro objetivo fue diseñada por cada equipo en la participación de los representantes de cada comunidad. Durante los últimos días del proyecto, los

participantes se reunieron con la comunidad en pequeños grupos dinámicos para discutir los problemas de salud descubiertos.

Actividades médicas:

1. Se tomó la tensión arterial y el pulso a toda la población.
2. Se midió la glicemia dos horas después de comer en personas mayores de 40 años y en los que por su historial pudieran ser diabéticos.
3. Se vacunó con DPT y Polio Oral a toda la población pediátrica.
4. Se hizo la prueba de tuberculina a toda persona mayor de tres meses que no hubiera sido positiva antes.
5. Se examinaron niños que en agosto ingresarían al primer grado.
6. Se examinó la excreta de personas en quienes se sospechaba anemia.
7. Se estudió la actitud y los conocimientos sobre la planificación familiar que tenían las mujeres en edad reproductiva.

Observaciones

Los problemas de salud encontrados, serán objeto de una publicación subsiguiente. Me limitaré a presentar las observaciones que hicimos de los estudiantes durante su experiencia.

Nuestra preocupación mayor era con los estudiantes entrantes a su primer año. No sabíamos en verdad que papel desempeñarían en equipos médicos y cuál habría de ser su aportación al grupo. Durante las primeras semanas se notó en ellos un grado de desconcierto y frustración que todos compartíamos. Nuestra frustración surgió porque desconocíamos la dinámica de la comunidad y carecíamos de asesoramiento médico y social. El libro era nuestro único consejero. Pero, muy pronto los estudiantes comenzaron a poner en práctica los métodos de entrevista y adquirieron una destreza especial para bregar con las personas adaptándose a su particular forma de ser. Muchos estudiantes se interesaron tanto en los análisis de excreta, que utilizaban sus horas libres nocturnas para examinar las muestras de todos los miembros de la familia asignados a ellos.

Paulativamente todos nos dimos cuenta que no era posible tratar parásitos sin darles a las personas una

De la Oficina de Educación Médica del Centro Médico de Mayagüez.

Interno, Centro Médico de Mayagüez.

explicación más completa sobre el ciclo de la vida del verme. Pudimos entonces insistir con éxito en el uso de zapatos y el correcto uso de los servicios sanitarios para el control efectivo de las infecciones parasitarias. Recalcamos el hecho que para la comunidad éste era el método más eficaz contra "las culebritas".

Nos dimos cuenta también de la importancia de educar a los individuos, de enseñarles a preocuparse por su salud. Concluimos que aunque el gobierno es llamado a garantizar los medios para tener una mejor salud, la comunidad comparte la responsabilidad de protegerse.

Buscamos un medio de medir el impacto de nuestra orientación sobre la comunidad. El número de asistencia a las reuniones generales nos pareció arbitrario. Confesamos que no encontramos ningún factor que nos indicase a ciencia cierta nuestro adelanto. El continuo reto ofrecido a los estudiantes por las comunidades estudiadas nos forzó a emplear gran parte de nuestro tiempo libre buscando información sobre distintos temas.

Al terminar las cuatro semanas los estudiantes se sintieron comprometidos con estas comunidades. Trabajan ahora en un plan de seguimiento para las mismas.

Conclusión

Estudiantes de medicina y recién graduados universitarios pueden realizar una positiva labor de orientación y prevención en comunidades aisladas. Esta experiencia es una orientación estimulante y formativa. Un mayor número de estudiantes provistos con más asesoramiento médico y social podrían aprender más y hacer una contribución de mayor importancia a la salud del pueblo puertorriqueño.

Resumen

Nueve estudiantes de medicina de primero, segundo y tercer año y un médico recién graduado diseñaron un proyecto de verano de orientación y prevención. Este fue dirigido a tres pequeñas comunidades en el área de Castañer. Durante las cuatro semanas que duró el proyecto los estudiantes experimentaron la frustración de sus limitados conocimientos pero aprendieron a conocer la comunidad y sus problemas de salud. Se concluye que este tipo de experiencia es estimulante y formativa para el estudiante y útil para comunidades aisladas. Con más asesoramiento médico y social los estudiantes podrían aprender más y hacer una contribución a la salud de mayor importancia.

Summary

Nine medical students in their first, second and third year and a newly graduated physician designed a summer project to provide medical orientation and prevention to isolated communities. Three small villages in the vicinity of Castañer were selected. During the four weeks that the project lasted the students felt the frustrations of their limited experience in this type of activity, but they learned to recognize the social and health problems of the region. This type of activity is not only formative and stimulating to the student, but is very useful to this type of community. If larger groups of medical students with better medical and social consultants and supervision were provided, this type of experience would be of greater didactic value and a greater contribution to the health of these communities would be possible.

EL CAMINO REAL

Ver un paciente sin un libro
es como ir a navegar sin brújula.
Leer un libro sin ver un paciente
es como nunca ir al mar.

Según William Osler

Desubicados y desorientados, muchos egresados del extranjero llegan de vuelta a su patria después de seis o más años de leer medicina. Los grandes tomos que cargan, las voluminosas notas de miles de conferencias magistrales ayudan poco al encontrarse con el paciente sudoroso y frío, con el angustioso dolor subesternal. El tendón, músculo y arteria que cortó un distraído machete en el cañaveral, no son susceptibles a destrezas nunca aprendidas en la demostración habilidosa y elegante del profesor insigne.

¿Se le habilitará al llegar a su patria? ¡No!

¿Que infamia pedagógica, que travestía diabólica descargar este joven en el pozo profundo y oscuro de la medicina asistencial! ¿Que amoralidad sádica permitirle que él, doctor principiante, “recete” 20 o 30 pacientes en dos horas, que lo guíe en cirugía el médico fracasado tres veces en la parte de anatomía y fisiología de la reválida, que “estudie” tras noches completas sin sueño en preparación para su tan codiciada certificación profesional!

¿Habrá algún otro camino? Sí.

En este mismo número el Dr. Alejandro Jiménez, egresado de la Universidad de Santiago de Compostela, detalla con candidez muy personal su experiencia en el curso Teórico-Práctico de Mayagüez. Es esta una rotación clínica, semejante a un cuarto año en hospitales universitarios donde conocimientos aprendidos adquieren nuevos significados, donde destrezas simples adquiridas y censuras medidas dan seguridad, confianza, reforman actitudes. Está bien emplazado el curso en el lejano oeste de Puerto Rico, a 151 kilómetros de la capital. La rotación empieza en cualquier área de la medicina y en cualquier momento. Aparte de terminar obligatoriamente a los diez meses, puede terminarse antes cuando el médico, ya maduro, cree haber obtenido la orientación deseada. La madurez profesional es, y siempre ha sido, una medida individual.

En la Villareal de Mayagüez conocimientos aplicables de la medicina y necesidades de cuerpo y del espíritu copulan libremente en habitaciones, pasillos y salones de clase. Noches con guardias que terminan a las diez, discusiones interminables con colegas que miran sin ansiedad la tarde que cae, son caminos más ciertos hacia la reubicación, la educación continuada y una formación médica profesional.

¡Sí! Hay una Via Appia para los egresados del extranjero, una experiencia teórico-práctica protegida y supervisada que sirva de puente entre el aula y la realidad del paciente. El doctor Jiménez, el primero en encontrar metas inesperadas en el trayecto de este nuevo sendero, ha abierto las posadas de este, El Camino Real.

José Ramírez Rivera, MD, FACP

CARTA AL EDITOR

GUEST EDITOR'S NOTE

This is an important message. The lack of attention to the needs of man which shocked this medical student occurs in varying degrees in all parts of the world. It is important that we recognize it and correct it here.

José Ramírez Rivera, MD

Dr. José Ramírez Rivera
Director of Medical Education
Mayagüez Medical Center
Mayagüez, Puerto Rico

Dear doctor Ramírez Rivera:

I want to thank you for the excellent opportunity that you have given three third year students of the New York University School of Medicine to refine our Spanish and to appreciate Puerto Rican culture. We have enjoyed the three weeks at the Medical Center and the week at the Health Center. The time spent in exploring Puerto Rico and meeting Puerto Ricans in their own environment will help us greatly in giving better care to Spanish-speaking patients in New York.

We would like to show our thanks for the opportunity given us by sharing with you — for positive reasons — this very strong reaction we have had to the human aspects of your medical care.

American medical students are witnessing an extensive modification in the relationship between doctors and their patients. As time goes on, patients are ceasing to be passive recipients of medical aid, mentally isolated from those who care for him or uninvolved in decisions concerning their health. Patients are becoming active participants in the doctor-patient relationship, continuously informed and mentally aware of their condition and what is being done for their management.

Despite the excellent quality of medical care afforded the patients in the Mayagüez Medical Center, I am disappointed to find that the changing relationship between doctor and patient found in the United States is for the most part absent here. Several specific examples may

clarify this point: All too often a doctor entered the room of a patient, said no more than a curt hello, performed an examination and left. There was no attempt at conversation, nothing was done to alleviate the patient's anxieties. Symptoms of disease were treated while the patient as an individual was neglected. Patients seemed to be "unusual gastric ulcers" or "interesting carcinomas".

A second seemingly trivial but very revealing fact was that some doctors smoked cigarettes while treating injured patients or rounding on patients. Can this casualness be considered courteous or considerate?

A third decidedly inappropriate practice to our view was extensive group discussion of a patient's diagnosis or management in front of the patient. Although some discussion among medical personnel must go on at the bedside, too little attention was paid to the patient's level of anxiety during these discussions. Why should non-therapeutic, anxiety producing conversations be conducted in the patient's presence?

In the mainland the increasing extent of communications between doctor and patient is partially the result of demands made by a more knowledgeable group of medical consumers. The Puerto Rican patient at the present time seems to be less medically sophisticated, less demanding of the health care delivery system. However, the lack of demand for better communications is no reason not to provide it. And certainly, consideration and respect for the ill patient, a concept so basic to the practice of medicine, should exist regardless of demand.

Although the medical care provided by the facilities of the Centro Médico of Mayagüez is impressive, improvement is always possible. I feel that a more humanistic view of the patient would improve greatly the quality of medical care.

Sincerely,
(Sgd) Jeffrey Lessing
Third Year Medical Student
New York University School of Medicine

NOTICIAS

MICOLOGIA MEDICA PARA TECNOLOGOS MEDICOS

El Laboratorio de Micología Tropical del Recinto Universitario de Mayagüez (salón C-301, Tel. 832-4040, Ext. 247), ofrecerá este año académico 1973-1974, tres cursos intensivos de 14 semanas de duración cada uno para entrenar Tecnólogos Médicos en Micología Médica.

Los cursos que estarán a cargo del Dr. Luis A. Roure, Cate-drático del RUM, se ofrecerán a ocho Tecnólogos Médicos en cada caso para un total de 24 para el primer año. Los tres grupos se reunirán respectivamente, del 14 de septiembre de 1973 al 21 de diciembre de 1973, del 11 de enero de 1974; durante 14 viernes consecutivos de 1:00 pm a 6:00 pm.

Este entrenamiento se hace posible mediante ayuda económica del Instituto Nacional de Salud de Maryland. Los interesados deben escribir una carta de solicitud al Dr. Luis A. Roure, Recinto Universitario de Mayagüez, Laboratorio de Micología Tropical, Mayagüez, Puerto Rico, 00708.

PEDIATRIC DERMATOLOGY SEMINAR, Fontainebleau Hotel, Miami Beach, Florida, February 22nd to 24th, 1974.

Address all inquiries to: Mrs. Frances Richardson, Post-graduate Education, Mount Sinai Medical Center, 4300 Alton Road, Miami Beach, Florida 33140.

PUERTO RICO INTERNAL MEDICINE SPECIALISTS TO MEET IN SEPTEMBER

PHILADELPHIA — The Puerto Rico Regional Meeting of the American College of Physicians will be held September 28-29, 1973, at the Puerto Rico Medical Association Building and the V. A. Hospital, San Juan, Puerto Rico.

The San Juan session is one of 35 area meetings sponsored for specialists in internal medicine and related fields by the 21,000-member American College of Physicians. It is designed to bring physicians up-to-date on medical advances and to provide continuing educational opportunities for members of the College throughout the United States and Canada.

In charge of arrangements for the Puerto Rico Regional Meeting is Elí A. Ramírez-Rodríguez, MD, 54 Club Drive, Garden Hills, Bayamón, Puerto Rico 00619.

ADVANCED WORKSHOP:

An advanced continuing education workshop in "PLASTIC

SURGERY OF THE NOSE: RHINOPLASTY AND RECONSTRUCTION" will be held September 29, 1973 to October 3, 1973, under the direction of M. Eugene Tardy, Jr., MD.

The course is jointly sponsored by the Department of Otolaryngology, University of Illinois Medical Center, the American Academy of Facial Plastic and Reconstructive Surgery, Inc., and Saint Joseph Hospital, Chicago, Illinois.

For brochure and applications, please write M. Eugene Tardy, Jr., MD, Course Director, Department of Otolaryngology, Eye and Ear Infirmary, 1855 W. Taylor, Chicago, Illinois 60612.

MYELOMA SYMPOSIUM

The Cancer Clinical Investigation Review Committee and the Clinical Investigations Branch of the National Cancer Institute are sponsoring a Symposium on Multiple Myeloma October 22-23, 1973, in Atlanta, Georgia at the Royal Coach Motor Hotel.

All physicians, house staff and medical students are welcome. For a detailed program and further information, write to:

Mrs. Jeanne Schaub, MW 408, John Sealy Hospital Building, University of Texas Medical Branch, Galveston, Texas 77550.

or

Mrs. Jeannette Steinbraker, Cancer Clinical Investigation Review Committee, National Cancer Institute, Room 10A03 Westwood Building, 5333 Westbard Avenue, Bethesda, Maryland 20016.

FROM HEW NEWS:

Proposed Medicare and Medicaid regulations to implement 1972 social security amendments on rules for payment of assigned supplementary medical insurance benefits, and on claims for practitioners' services provided under a State medical assistance plan were announced today by HEW Secretary Gaspar W. Weinberger.

Under the amendments, such Medicare and Medicaid payments are prohibited to anyone other than the physician or other person who furnished the services with two exceptions. One exception permits payment to the employer of the physician or other person who furnished the service, if the doctor or other person is required to turn over his fees for the service to the employer.

The second exception permits payment to the facility in which the service is provided, if there is a contractual

arrangement between the facility and the person furnishing the service under which the facility bills for the service.

The proposed regulation recognizes that the intent of the 1972 amendments was not to bar direct payment to a foundation, association, plan, or contractor which provides and administers health care through an organized health care delivery system.

The proposal also defines "facility" as being a hospital or other institution which furnishes health care services to in-patients, and provides that a "health care delivery system" includes — but is not limited to—an organized medical group clinic and a group practice prepayment plan.

Interested parties have 30 days from June 27, 1973, the date of publication of the proposed regulations in the *Federal Register*, to submit comments.

Regulations governing the conditions under which Medicare can help pay for certain services provided by licensed chiropractors and independent physical therapists were proposed today by the Department of Health, Education, and Welfare.

Under the proposed regulations Medicare will help pay for manual manipulation of the spine only to correct a subluxation which can be shown by x-rays to exist and which has caused a condition for which manipulation is appropriate treatment. No reimbursement may be made for x-rays or other diagnostic or therapeutic services provided by chiropractors.

To be certified for Medicare reimbursement, chiropractors must be licensed, must have completed an extensive course of study including anatomy, physiology, chemistry, and principles and practice of chiropractic, including clinical instruction, and must have passed an examination by the State's chiropractic examiners.

The proposed regulations also provide that Medicare will help pay for services furnished by an independent physical therapist in his office or in the patient's home, up to a maximum of \$100 of incurred expenses in a year.

Interested parties have 30 days from June 29, 1973, the date of publication for the proposed regulations in the *Federal Register*, to submit comments.

COURSE IN POSTGRADUATE GASTROENTEROLOGY —

The American College of Gastroenterology announces that its Annual Course in Postgraduate Gastroenterology will be given at The Biltmore Hotel in Los Angeles, Calif., on Thursday, Friday and Saturday, 25, 26, 27 October 1973, immediately following the 38th Annual Convention of the College which will also be held there on 22, 23, 24 October.

Further information and enrollment may be obtained from:

The American College of Gastroenterology
299 Broadway
New York, N. Y., 10007 USA

CURSO DE ORIENTACION PARA EGRESADOS DEL EXTRANJERO:

El Centro Médico de Mayagüez ofrece un curso de orien-

tación de medicina aplicada, para egresados de escuelas extranjeras que no hayan aprobado la reválida ni tengan el ECFMG.

Este curso teórico-práctico está diseñado para crear una transición supervisada entre el aula y la atención al paciente. Está compuesto de rotaciones por los cuatro servicios clínicos. La rotación empieza en cualquiera de los servicios escogido por el solicitante y en cualquier momento; aparte de terminar obligatoriamente a los 10 meses, puede terminarse cuando el médico haya tenido la orientación deseada. Hay un número limitado de becas de \$400.00 mensuales. Algunos Alcaldes de la Región Oeste, ofrecen \$200.00 de becas adicionales para aquellos médicos que se comprometan hacer el año de servicio público en sus pueblos al terminar el internado.

Solicite informes al Dr. José Ramírez Rivera, Director de Educación Médica e Investigaciones Clínicas, Centro Médico, Mayagüez, Puerto Rico 00708.

JAMA EDITORIAL STRESSES OPERATING ROOM SAFETY

CHICAGO—A plea for greater care in checking electrical devices in hospital operating rooms is voiced in an editorial in an issue of the *Journal of the American Medical Association*.

"The life-saving results achieved by a team of skillful surgeons and anesthetists, reinforced by a well-trained team of nurses and operating room personnel, may be nullified by a simple and avoidable accident of a mechanical or electrical nature in the operating room," the editorial says. The author is Zenonas Danilevicius, M. D., a senior editor of the *Journal*.

"The most difficult and invisible dangers to the patient lurk in the electrical system of the operating room, in its electrical and electronic equipment."

The hazard of static electricity is well known, and is universally avoided by use of materials, clothing, equipment shoes and flooring material that does not conduct electricity.

A danger arises with the use of high-powered electrical equipment, especially for electrosurgery or electrocautery, the editorial reports. Cited is a situation in one hospital in which nine patients suffered burns at the sites of electrocardiograph electrodes (heart monitoring equipment) within a period of ten months.

Causes of the burns were broken ground wires, defective rectifiers, improper equipment, improper use of active electrodes, capacitive coupling of cables, and radio frequency current division. The staff made a detailed study of the electrical system and the defects were corrected.

One case is indicative of the problems sometimes encountered. During surgery the electrocardiographic tracing did not function properly and the electrical connection was transferred from one wall plug to another. The anesthesiologist felt a shock in the hand in checking the patient's pulse, the patient made a sudden jerking movement and the pulse stopped abruptly. The doctor immediately pulled out the plug and began first aid. The patient made a full recovery. A follow-up investigation revealed that an improperly wired electrocardiographic monitor had been in use for some time. Also some of the wall sockets in the operating room had reversed polarity. All defects were immediately corrected.

"Isolated power systems are highly recommended for the patient care areas in all hospitals. The isolation transformers and the line-isolation monitors are also recommended as a

protection against macroshock hazards. Proper grounding of all the equipment and of all the electrical systems is also a must. Frequent checks of all electrical aspects of the operating rooms by skilled engineer-surgeon teams would be a good measure of protection."

ELECTROCARDIOGRAM SOMETIMES MISSES CORONARY ARTERY DISEASE

CHICAGO—The grim tale of the patient who undergoes a complete physical examination, is given a clean bill of health, then drops dead of heart attack as he leaves the doctor's office is widely known.

This doesn't happen often, but it does happen.

A research group from the Institute for Cardiovascular Diseases at Good Samaritan Hospital, Phoenix, Ariz., tells why in an article in the June 11th issue of the *Journal of the American Medical Association*.

The electrocardiogram — the monitoring machine on which the doctor depends to determine heart problems — does not always reliably predict the extent of coronary artery disease, the Arizona doctors report.

The electrocardiogram (ECG) will show a normal tracing in a substantial number of patients with significant triple-vessel coronary artery disease, when the ECG is taken in the usual resting position, supine on an examining table in the doctor's office or hospital, they say.

In a study conducted in the Phoenix hospital, the researchers found that 17 of 106 patients known to have triple-vessel coronary artery disease had completely normal ECGs. Three patients with 100 percent obstruction had normal readings.

STRICT CONTROL URGED FOR "LOVE DRUG" PILLS

CHICAGO—The "Love Drug" is under fire this spring on several fronts as a dangerous, addictive and potentially fatal "downer" pill.

The "Love Drug" — so called because of supposed aphrodisiac qualities — is known to medicine as methaqualone. To the American public it is dispensed under such trade names as Quaalude, Optimil, Sopor, Parest, Somnafac and Biphetamine T. It is a sleeping pill.

The American Medical Association last month voiced its support for strict control of the drug. The U. S. Attorney General and the Secretary of Health, Education and Welfare have taken action to place the drug under sharp restrictions.

Two separate articles — from California and from New York — together with an editorial, all dealing with methaqualone abuse, appear in the June 11th issue of the *Journal of the American Medical Association*.

Emil F. Pascarelli, M. D., of Roosevelt Hospital, New York City, writes of "Methaqualone Abuse, the Quiet Epidemic." Four staffers from the Haight-Ashbury Free Medical Clinic in San Francisco report on "Methaqualone Abuse: 'Luding Out.'" The JAMA editorial, by John R. Lewis of the AMA's Department of Drugs and E. M. Steindler of the association's Department of Mental Health, points out that AMA warned physicians as early as 1967 of potential harmful effects of the drug.

Incidentally, the so-called "Love Drug" actually decreases sexual capacity because of its depressant effect. "Luding Out" refers to the impact of the drug on users.

The San Francisco study cites several cases of patients treated for the effects of methaqualone abuse. It concludes:

"From the patients we treated at the Drug Detoxification Project, we conclude that methaqualone abuse and addiction is qualitatively equivalent to that of the short-acting barbiturates. We further question other promotional claims of methaqualone, and do not find it superior to other sedative-hypnotics already flooding the drug market."

The Haight-Ashbury report is by Darryl S. Inaba, Pharm. D.; George R. Gay, M. D.; John A. Newmeyer, Ph.D., and Craig Whitehead, M. D.

Dr. Pascarelli declares:

"Abuse of the nonbarbiturate hypnotic, methaqualone, has quietly reached the proportions of a countrywide epidemic among students and others. Methaqualone abusers, caught up in its 'love drug' mystique and seeking a dissociative 'high', are oblivious to many of its dangers. Experience in Europe and elsewhere indicates that the drug has a marked potential for producing dependence and causes a severe withdrawal syndrome."

The *Journal* editorial says:

"Based on accumulating case reports, stories in the press, and experience in other countries, the AMA's Committee on Alcoholism and Drug Dependence and Department of Drugs have recommended the imposition of controls. Because of methaqualone's relatively limited usefulness in medicine, they have proposed, along with the Bureau of Narcotics and Dangerous Drugs and the Food and Drug Administration, that the drug be placed in Schedule II, which provides for production quotas and for unrefillable prescriptions.

"Methaqualone, in addition to being widely abused, has no advantage over other sedatives, may produce serious toxic reactions, and has a potential for both physical and psychological dependence. It cannot be considered, therefore, to be a drug essential to medical practice."

KARATE CHOP CAUSES SERIOUS DAMAGE TO LIVER

CHICAGO—Warning: A karate chop may be highly dangerous to your liver.

Karate is a fast-growing participation sport due partially to the medical emphasis on the benefits of physical fitness and the individual desire for self-protection in the face of high municipal crime rates, says a communication in the June 4th issue of the *Journal of the American Medical Association*.

John Davis Cantwell, M. D., and James T. King, Jr., M. D., of Georgia Baptist Hospital, Atlanta, describe the case of a 39-year-old woman who suffered severe liver damage from a combination of blows to the abdomen during her second lesson in karate. She suffered pain at the time, but X-rays showed no broken bones, and she was given only mild pain killers. Six weeks later she was hospitalized, severely ill. Surgery revealed the liver was lacerated and swollen to twice normal size. The damage was repaired and she recovered, after three weeks in the hospital.

The liver ranks second only to the spleen as the organ

most commonly injured by a sharp blow to the abdomen, the doctors report. The death rate is high if treatment is delayed. In the case reported, the severe symptoms did not show up until six weeks after the injury. Early surgery and treatment are generally recommended for suspected liver injury, they say.

"This is not to condemn karate but rather to call attention to the potential injury to an abdominal organ from a forceful blow. Closer supervision of participants is advised," they conclude.

"TENNIS TOE" IS NEW HEALTH PROBLEM FOR ATHLETES

CHICAGO—Weekend athletes now have another medical problem to worry about — tennis toe.

Tennis elbow has long been known to be a vocational hazard of tennis players. It's similar to pitcher's elbow in baseball.

And now comes tennis toe, mentioned in a report in the June issue of *Archives of Dermatology*, a publication of the American Medical Association.

Richard C. Gibbs, M. D., of New York, reports:

"For the past few years I have been impressed by the number of tennis players who complain of pain in one or more of their toes. The pain is associated with the appearance of hemorrhage beneath their toenails. The toe affected is that which extends furthest."

Sometimes this is the big toe, sometimes the second toe, sometimes both extend about the same.

"The explanation I have always held for tennis toe is that in tennis one is frequently stopping abruptly and the forward motion of the body propels the toes into the box toe and tip of the sneakers."

NEWS RELEASE FROM SMITH, KLINE & FRENCH LABORATORIES:

How do you locate the estimated 11 million unsuspecting Americans whose undiagnosed condition makes them leading candidates for heart attack, stroke and untimely death?

When you do locate the 11 million, the majority may feel they are completely healthy. How do you convince them of the seriousness of their condition?

And how do you educate them so that they will remain on the regimen necessary to relieve that condition?

These questions challenged the National High Blood Pressure Education Program when it was created in 1972 by government and voluntary health agencies to prevent death and disability from hypertension. One of the innovative solutions to the challenge is the utilization of Smith Kline

& French Laboratories' Professional Representatives to call on the nation's physicians, supplying them with information on the campaign, including material to educate the hypertensive patient.

The campaign directed at physicians will get underway in mid-June. The information package will detail the incidence and morbidity of hypertension while emphasizing that the disease can be readily controlled —once diagnosis is made.

OBRAS INCORPORADAS RECIENTEMENTE EN LA BIBLIOTECA DE LA UNIVERSIDAD DE PUERTO RICO, RECINTO DE CIENCIAS MEDICAS (RECENT ACQUISITIONS AT THE LIBRARY OF THE UPR MEDICAL SCIENCES CAMPUS)

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LISTA DE ANUNCIANTES

1. Burroughs Wellcome — Neosporin, Empirin \bar{c} Codeine
2. Ciba — Vioform HC
3. Eaton Labs. — Macrodantin
4. Geigy Pharm. — DBI-TD
5. Pharm. Mfrs. — Intitutional
6. Roche — Efudex, Librium, Valium

7. Rorer — Maalox
8. Searle — Flagyl
9. Stuart Pharm. — Mylanta
10. Syntex — Neo-Mull-Soy
11. Upjohn — Unicap Therapeutic

Dx: Hiatal Hernia

Rx: Maalox[®]

Maalox[®] relieves the symptoms of hiatal hernia by neutralizing gastric hyperacidity. It doesn't constipate. And its taste is pleasant, nonfatiguing—all important considerations in the treatment of a long-term condition like hiatal hernia.

In short, Maalox is the kind of antacid that makes symptomatic relief of hiatal hernia as decisive as its diagnosis.

Maalox[®] Suspension

(Magnesia and Alumina Oral Suspension, Rorer)
(5 fl. oz. [plastic bottle] and 12 fl. oz.).

Maalox[®] No. 1 Tablets (0.4 Gm.)

—no sugar and low in sodium.

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—the "chew" tablet with double antacid action.

Maalox[®]

(Magnesia and Alumina Oral Suspension, Rorer)

the number one antacid



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What's on your patient's face...

may be more important than his chief complaint

Patient P.T.* seen on 3/29/67 shows typical lesions of moderately severe keratoses. Note residual scarring on ridge of nose from previous cryosurgical and electrosurgical procedures.



Patient P.T.* seen on 6/12/67, seven weeks after discontinuation of 5% FU cream. Reaction has subsided. Residual scarring not seen except that due to prior surgery. Inflammation has cleared and face is clear of keratotic lesions.

*Data on file,
Hoffmann-La Roche
Inc., Nutley, N.J



The lesions on his face are solar/actinic— so-called "senile" keratoses... and they may be premalignant.

Solar, actinic or senile keratoses

These lesions may be called by several names, but they usually can be identified by the following characteristics. The typical lesion is flat or slightly elevated, of a brownish or reddish color, papular, dry, rough, adherent and sharply defined. They commonly occur as multiple lesions, chiefly on the exposed portions of the skin.

Sequence of therapy— selectivity of response

After several days of therapy with Efudex® (fluorouracil), erythema may begin to appear in the area of the lesions; this reaction usually reaches its height of unsightliness and discomfort within two weeks, declining after discontinuation of therapy. This reaction occurs in affected areas. Since the response is so predictable, lesions that do not respond should be biopsied.

Acceptable results

Treatment with Efudex provides highly favorable cosmetic results. Incidence of scarring is low. This is particularly important with multiple facial lesions. Efudex should be applied with care near the eyes, nose and mouth.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Multiple actinic or solar keratoses.

Contraindications: Patients with known hypersensitivity to any of its components.

Warnings: If occlusive dressing used, may increase inflammatory reactions in adjacent normal skin. Avoid prolonged exposure to ultraviolet rays. Safe use in pregnancy not established.

Precautions: If applied with fingers, wash hands immediately. Apply with care near eyes, nose and mouth. Lesions failing to respond or recurring should be biopsied.

Adverse Reactions: Local—pain, pruritus, hyperpigmentation and burning at application site most frequent; also dermatitis, scarring, soreness and tenderness. Also reported—insomnia, stomatitis, suppuration, scaling, swelling, irritability, medicinal taste, photosensitivity, lacrimation, leukocytosis, thrombocytopenia, toxic granulation and eosinophilia.

Dosage and Administration: Apply sufficient quantity to cover lesion twice daily with nonmetal applicator or suitable glove. Usual duration of therapy is 2 to 4 weeks.

How Supplied: Solution, 10-ml drop dispensers—containing 2% or 5% fluorouracil on a weight/weight basis, compounded with propylene glycol, tris(hydroxymethyl)aminomethane, hydroxypropyl cellulose, parabens (methyl and propyl) and disodium edetate.

Cream, 25-Gm tubes—containing 5% fluorouracil in a vanishing cream base consisting of white petrolatum, stearyl alcohol, propylene glycol, polysorbate 60 and parabens (methyl and propyl).



Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, N.J. 07110

This patient's lesions were resolved with

Efudex®

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5% cream/solution...a Roche exclusive

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Whenever the symptoms diarrhea, colic, vomiting, rhinorrhea, anorexia or eczema are evident, consider milk intolerance—then consider Neo-Mull-Soy.

Protein, fat and carbohydrate levels approximating those of human milk.

Methionine-supplemented to enhance protein efficiency.

Low renal solute load.

No corn sugars.

Comparable to cow's milk formulas in supporting growth and development.

**ALL THIS...
AND MILK-WHITE,
TOO.**



NEO-MULL-SOY

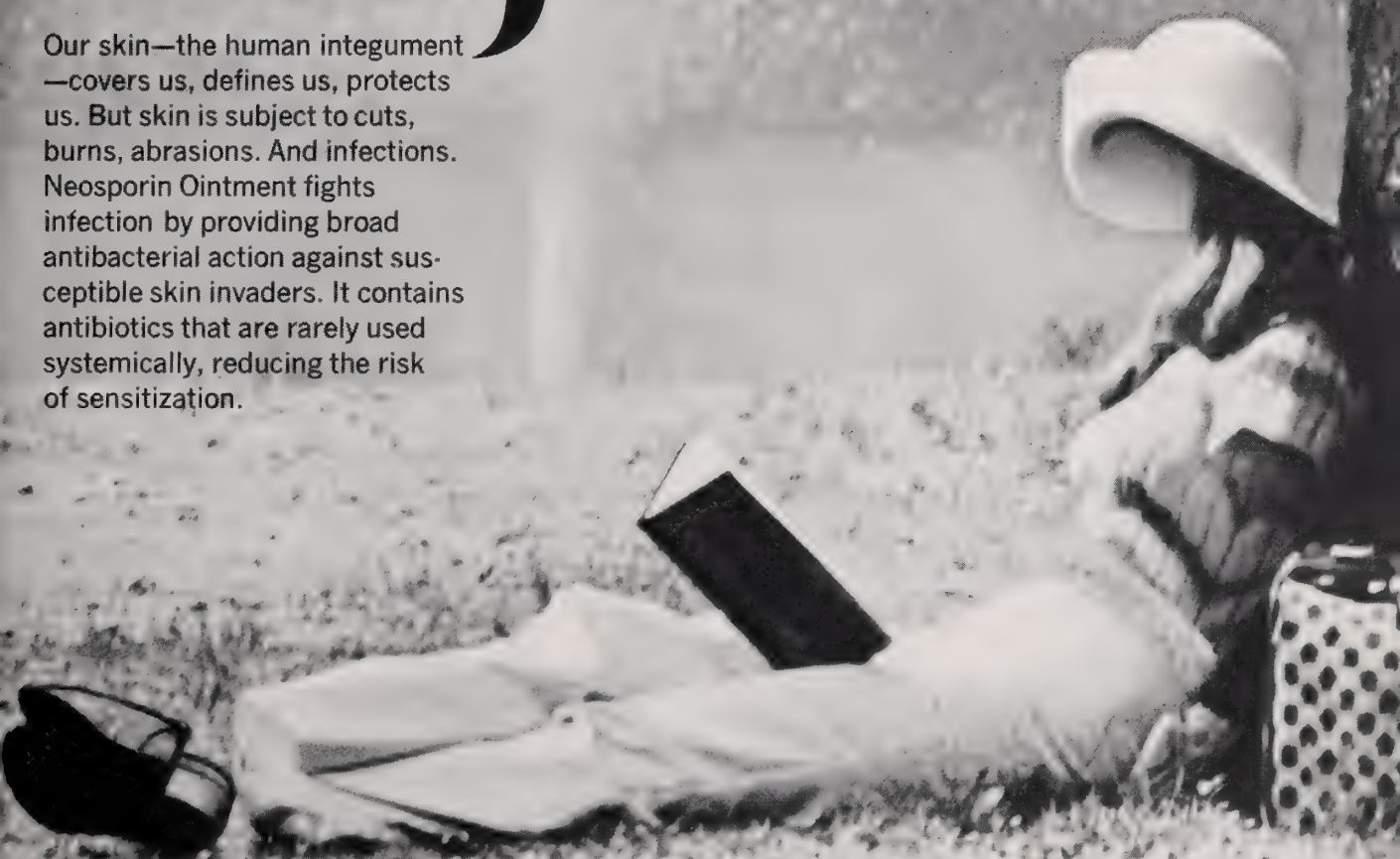
Soy Protein Isolate Formula

SYNTEX

SYNTEX LABORATORIES, INC.
NUTRITIONAL PRODUCTS DIV.
PALO ALTO, CALIFORNIA 94304

Integument!

Our skin—the human integument—covers us, defines us, protects us. But skin is subject to cuts, burns, abrasions. And infections. Neosporin Ointment fights infection by providing broad antibacterial action against susceptible skin invaders. It contains antibiotics that are rarely used systemically, reducing the risk of sensitization.



INDICATIONS: *Therapeutically*, used as an adjunct to appropriate systemic therapy for topical infections, primary or secondary, due to susceptible organisms, as in:

- infected burns, skin grafts, surgical incisions, otitis externa
- primary pyodermas (impetigo, ecthyma, sycosis vulgaris, paronychia)
- secondarily infected dermatoses (eczema, herpes, and seborrheic dermatitis)
- traumatic lesions, inflamed or suppurating as a result of bacterial infection.

Prophylactically, the ointment may be used to prevent bacterial contamination in burns, skin grafts, incisions, and other clean lesions. For abrasions, minor cuts and wounds accidentally incurred, its use may prevent the development of infection and permit wound healing.

CONTRAINDICATIONS: Not for use in the external ear canal if the eardrum is perforated. This product is contraindicated in those individuals who have shown hypersensitivity to any of the components.

PRECAUTION: As with other antibiotic preparations, prolonged use may result in overgrowth of nonsusceptible organisms and/or fungi. Appropriate measures should be taken if this occurs. Articles in the current medical literature indicate an increase in the prevalence of persons allergic to neomycin. The possibility of such a reaction should be borne in mind.

Complete literature available on request from Professional Services Dept. PML.

NEOSPORIN[®] Ointment

(POLYMYXIN B-BACITRACIN-NEOMYCIN)

Each gram contains: Aerosporin[®] brand Polymyxin B Sulfate 5,000 units; zinc bacitracin 400 units; neomycin sulfate 5 mg. (equivalent to 3.5 mg. neomycin base); special white petrolatum q.s. In tubes of 1 oz. and ½ oz. and ¼ oz. (approx.) foil packets.



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Research Triangle Park
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We're not against all her E. coli...

only the E. coli in her
urinary tract



Macrochantin (nitrofurantoin macrocrystals) is exceptionally effective against E. coli. But it confines its antibacterial action to the urinary tract. It is indicated for the treatment of cystitis,* pyelitis* and pyelonephritis*...nothing else.

Macrochantin is not indicated for therapy of any systemic infection. And it does not suppress normal bac-

**Basic in cystitis*, pyelitis*,
pyelonephritis***

The one-tract action of

Macrochantin® Capsules
(nitrofurantoin macrocrystals) 50mg/100mg.

Indications: Macrochantin (nitrofurantoin macrocrystals) is indicated for the treatment of pyelonephritis, pyelitis and cystitis due to E. coli, enterococci, Staph. aureus or a small percentage of strains of Pseudomonas, when demonstrated to be susceptible by in vitro susceptibility testing. Also for treatment of such infections when due to some susceptible strains of Klebsiella-Aerobacter and Proteus. It is not indicated for treatment of associated renal cortical or perinephric abscesses, systemic infections or prostatitis, or in any genitourinary tract infections other than pyelonephritis, pyelitis and cystitis.

Contraindications: Anuria, oliguria or extensive impairment of renal function is a contraindication. The drug is contraindicated for infants under one month and in pregnant patients at term. The drug should not be administered to persons who have shown hypersensitivity to nitrofurantoin.

Warnings: Macrochantin may cause hemolytic anemia of the primaquine sensitivity type, apparently linked to a glucose-6-phosphate dehydrogenase deficiency. This deficiency is found in 10 per cent of Negroes and in a small percentage of ethnic groups of Mediterra-

nean and Near-Eastern origin. Such patients should be observed closely while receiving nitrofurantoin. Discontinue the drug at any sign of hemolysis. Hemolysis ceases on withdrawal. Superinfections may occur, most commonly due to Pseudomonas.

Usage in pregnancy: THE SAFETY OF NITROFURANTOIN DURING PREGNANCY AND LACTATION HAS NOT BEEN ESTABLISHED. IT SHOULD NOT BE USED IN WOMEN OF CHILDBEARING POTENTIAL UNLESS THE EXPECTED BENEFITS OUTWEIGH THE POSSIBLE HAZARDS.

Precautions: Peripheral neuropathy may occur. A fatality has been reported. Predisposing conditions such as renal impairment, anemia, diabetes, electrolyte imbalance, vitamin B deficiency and debilitating disease may enhance such occurrence.

Adverse reactions: Nausea, emesis and diarrhea may occur; reduction in dosage may alleviate these symptoms. Sensitization appearing as cutaneous eruptions or pruritus has occurred. Hypersensitivity reactions resulting in nonfatal anaphylaxis, angioedema, pulmonary infiltration with pleural effusion and eosinophilia have been reported. Other possible

terial flora elsewhere in the body. (As with other antibacterials, superinfections may occur, but these are limited to the urinary tract. Pseudomonas is the organism most commonly implicated.)

Macrochantin works against a majority of urinary tract pathogens, including some strains of Proteus and Klebsiella-Aerobacter; however, only a small percentage of strains of Pseudomonas are susceptible.

*Due to susceptible organisms.

reactions are chills, fever, jaundice, asthmatic symptoms and hypotension. Occasionally headache, dizziness, nystagmus, vertigo, drowsiness, malaise and muscular aches have occurred. Transient alopecia has been reported. Leukopenia, including granulocytopenia, has been reported rarely. The blood picture has returned to normal following cessation of therapy. As with other antimicrobial agents, superinfections by resistant organisms may occur. With Macrochantin, however, these are limited to the genitourinary tract because suppression of normal bacterial flora elsewhere in the body does not occur.

Dosage: Adult: 50 to 100 mg. four times a day.

Supplied: Macrochantin (nitrofurantoin macrocrystals) Capsules of 50 mg. and 100 mg.

EATON PRODUCT CODE—For easy product identification and verification—Macrochantin Capsules 50 mg. (F03), 100 mg. (F04).



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10 vitaminas combinadas con 7 minerales

Cada tableta contiene:

Vitamina A	1.5 mg.
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Mononitrato de Tiamina (B-1)	10 mg.
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Acido Ascórbico (C) (como ascorbato de sodio)	300 mg.
Niacinamida	100 mg.
Clorhidrato de Piridoxina (B-6)	2 mg.
Pantotenato de Calcio	20 mg.
Cobalamina (B-12) (como concentrado de cobalamina)	20 mg.
Vitamina E	30 Unidades Internacionales
Hierro (a partir de 50 mg. de sulfato ferroso)	10 mg.
Yodo (como yoduro de potasio)	0.15 mg.
Calcio (como carbonato)	50 mg.
Cobre (como sulfato)	1 mg.
Manganeso (como sulfato)	1 mg.
Magnesio (como sulfato)	6 mg.
Potasio (como sulfato)	5 mg.

Posología: Adultos y niños mayores de 6 años – 1 tableta diaria.

Presentación: Frascos de 30 y 90

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How strong must a tranquilizer be for severe anxiety?

As strong as Librium® 25 mg (chlordiazepoxide HCl)



The achievement of desired therapeutic results is often a function of the dosage strength as well as the drug's intrinsic action. Thus, when anxiety is *severe*, the 25-mg strength of Librium frequently provides the necessary antianxiety action with a minimum of unwanted adverse reactions. Librium 25 mg is a convenient dosage form for the relief of severe, incapacitating anxiety, specifically formulated to supplement your counsel and reassurance.

Benefits-to-risks ratio permits higher dosage

For over 13 years, Librium has been recognized for its excellent benefits-to-risks ratio, an asset in the *higher* dosage ranges as in more common clinical applications. Thus, the frequency of dosage with Librium 25 mg can be flexibly adjusted to the needs and response of the individual patient, up to 100 mg daily if required. Total daily dosage for the elderly and debilitated should not exceed 20 mg. When severe anxiety has been reduced, Librium dosage should be correspondingly reduced or discontinued entirely.



basic support
in severe anxiety
Librium® 25 mg
(chlordiazepoxide HCl)
1 capsule t.i.d./q.i.d.



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Before prescribing, please consult complete product information, a summary of which follows:

Indications: Relief of anxiety and tension occurring alone or accompanying various disease states.

Contraindications: Patients with known hypersensitivity to the drug.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates have been reported. Use of any drug in pregnancy, lactation, or in women of childbearing age requires that its potential benefits be weighed against its possible hazards.

Precautions: In the elderly and debilitated and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

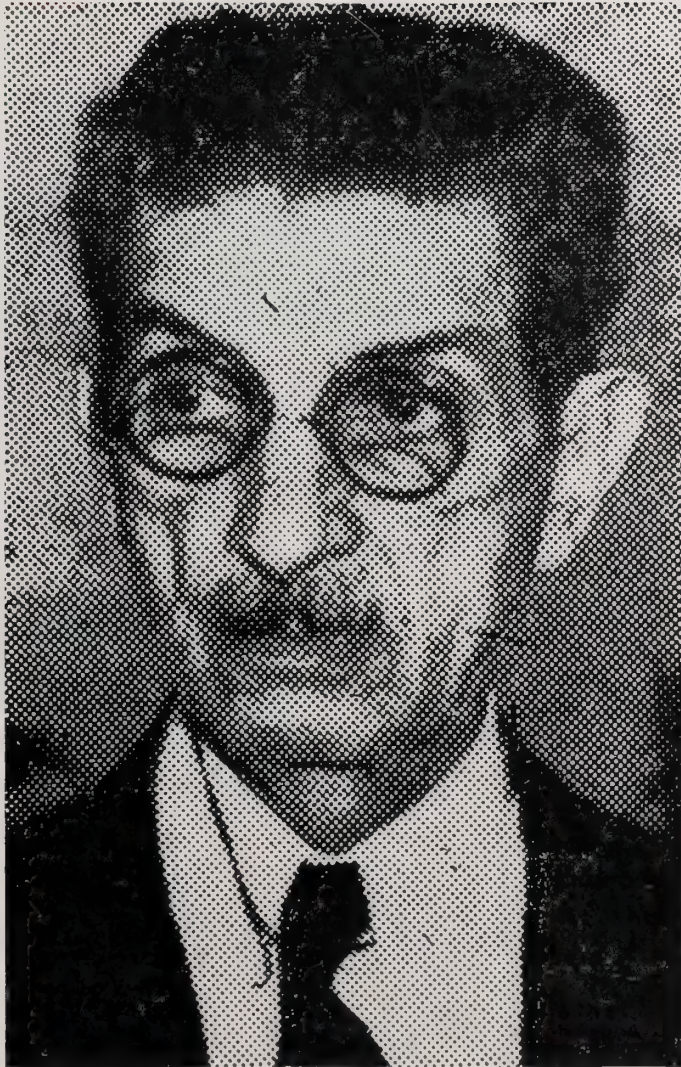
Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruption, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increase and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

Supplied: Librium® Capsules containing 5 mg, 10 mg or 25 mg chlordiazepoxide HCl. Libritabs® Tablets containing 5 mg, 10 mg or 25 mg chlordiazepoxide.

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DR. MANUEL QUEVEDO BAEZ
1865 - 1955



Everybody experiences psychic tension.



Most people can handle this tension.



Some people develop excessive psychic tension and need your counseling,



and a few may need counseling
and the psychotropic action of Valium® (diazepam).

Before deciding to make Valium (diazepam) part of your treatment plan, check on whether or not the patient is presently taking drugs and, if so, what his response has been. Along with the medical and social history, this information can help you determine initial dosage, the possibility of side effects and the ultimate prospects of success or failure.

While Valium can be a most helpful adjunct to your counseling, it should be prescribed only as long as excessive psychic tension persists and should be discontinued when you decide it has accomplished its therapeutic task. In general, when dosage guidelines are followed, Valium is well tolerated (see Dosage). For convenience it is available in 2-mg, 5-mg and 10-mg tablets.

Drowsiness, fatigue and ataxia have been the most commonly reported side effects.

Until response is determined, patients receiving Valium should be cautioned against engaging in hazardous occupations requiring complete mental alertness, such as driving or operating machinery.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

Dosage: Individualize for maximum beneficial effect. *Adults:* Tension, anxiety and psychoneurotic states, 2 to 10 mg b.i.d. to q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed; adjunctively in skeletal muscle spasm, 2 to 10 mg t.i.d. or q.i.d.; adjunctively in convulsive disorders, 2 to 10 mg b.i.d. to q.i.d. *Geriatric or debilitated patients:* 2 to 2½ mg, 1 or 2 times daily initially, increasing as needed and tolerated. (See Precautions.) *Children:* 1 to 2½ mg t.i.d. or q.i.d. initially, increasing as needed and tolerated (not for use under 6 months).

Supplied: Valium® (diazepam) Tablets, 2 mg, 5 mg and 10 mg; bottles of 100 and 500. All strengths also available in Tel-E-Dose® packages of 1000.



Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, N.J. 07110

Valium® (diazepam)

To help you manage excessive psychic tension

What's on your patient's face...

may be more important than his chief complaint

Patient P.T.* seen on 3/29/67 shows typical lesions of moderately severe keratoses. Note residual scarring on ridge of nose from previous cryosurgical and electrosurgical procedures.



Patient P.T.* seen on 6/12/67, seven weeks after discontinuation of 5% FU cream. Reaction has subsided. Residual scarring not seen except that due to prior surgery. Inflammation has cleared and face is clear of keratotic lesions.

*Data on file,
Hoffmann-La Roche
Inc., Nutley, N.J



The lesions on his face are solar/actinic— so-called "senile" keratoses... and they may be premalignant.

Solar, actinic or senile keratoses

These lesions may be called by several names, but they usually can be identified by the following characteristics. The typical lesion is flat or slightly elevated, of a brownish or reddish color, papular, dry, rough, adherent and sharply defined. They commonly occur as multiple lesions, chiefly on the exposed portions of the skin.

Sequence of therapy— selectivity of response

After several days of therapy with Efudex® (fluorouracil), erythema may begin to appear in the area of the lesions; this reaction usually reaches its height of unsightliness and discomfort within two weeks, declining after discontinuation of therapy. This reaction occurs in affected areas. Since the response is so predictable, lesions that do not respond should be biopsied.

Acceptable results

Treatment with Efudex provides highly favorable cosmetic results. Incidence of scarring is low. This is particularly important with multiple facial lesions. Efudex should be applied with care near the eyes, nose and mouth.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Multiple actinic or solar keratoses.

Contraindications: Patients with known hypersensitivity to any of its components.

Warnings: If occlusive dressing used, may increase inflammatory reactions in adjacent normal skin. Avoid prolonged exposure to ultraviolet rays. Safe use in pregnancy not established.

Precautions: If applied with fingers, wash hands immediately. Apply with care near eyes, nose and mouth. Lesions failing to respond or recurring should be biopsied.

Adverse Reactions: Local—pain, pruritus, hyperpigmentation and burning at application site most frequent; also dermatitis, scarring, soreness and tenderness. Also reported—insomnia, stomatitis, suppuration, scaling, swelling, irritability, medicinal taste, photosensitivity, lacrimation, leukocytosis, thrombocytopenia, toxic granulation and eosinophilia.

Dosage and Administration: Apply sufficient quantity to cover lesion twice daily with nonmetal applicator or suitable glove. Usual duration of therapy is 2 to 4 weeks.

How Supplied: Solution, 10-ml drop dispensers—containing 2% or 5% fluorouracil on a weight/weight basis, compounded with propylene glycol, tris(hydroxymethyl)-aminomethane, hydroxypropyl cellulose, parabens (methyl and propyl) and disodium edetate.

Cream, 25-Gm tubes—containing 5% fluorouracil in a vanishing cream base consisting of white petrolatum, stearyl alcohol, propylene glycol, polysorbate 60 and parabens (methyl and propyl).



Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, N.J. 07110

This patient's lesions were resolved with

Efudex® fluorouracil/Roche®

5% cream/solution...a Roche exclusive

BOLETIN

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El Boletín acepta para su publicación artículos relativos a medicina y cirugía y las ciencias afines. Igualmente acepta artículos especiales y correspondencia que pudiera ser de interés general para la profesión médica. El artículo, si se aceptara, será con la condición de que se publicará únicamente en esta revista. La AMPR no se hace responsable de las opiniones y declaraciones vertidas por los autores y sus puntos de vista no necesariamente representan aquellos de la AMPR; cualquier relación con la política oficial es coincidencia.

Second Class postage paid at San Juan, P. R.

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CUBIERTA DEL MES DE SEPTIEMBRE: DR. MANUEL QUEVEDO BAEZ (1865 - 1955)

(Con motivo de celebrarse en el mes de Septiembre el "Día del Médico" creímos conveniente publicar la fotografía del Dr. Manuel Quevedo Báez, Fundador y Primer Presidente de la Asociación Médica de Puerto Rico)



Bobo's back at the big top

After a rheumatoid arthritic flare-up.

Important Note: This drug is not a simple analgesic. Do not administer casually. Carefully evaluate patients before starting treatment and keep them under close supervision. Obtain a detailed history, and complete physical and laboratory examination (complete hemogram, urinalysis, etc.) before prescribing and at frequent intervals thereafter. Carefully select patients, avoiding those responsive to routine measures, contraindicated patients or those who cannot be observed frequently. Warn patients not to exceed recommended dosage. Short-term relief of severe symptoms with the smallest possible dosage is the goal of therapy. Dosage should be taken with meals or a full glass of milk. Subcutaneous capsules for tablets if dyspeptic symptoms occur. Patients should discontinue the drug and report immediately any sign of: fever, sore throat, oral lesions, symptoms of blood dyscrasia; dyspepsia, epigastric pain, symptoms of anemia, black or tarry stools or other evidence of intestinal ulceration or hemorrhage, skin reactions, significant weight gain or edema. A one-week trial period is adequate. Discontinue in the absence of a favorable response. Restrict treatment periods to one week in patients over sixty.

Indications: Acute gouty arthritis, rheumatoid arthritis, ankylosing spondylitis.

Contraindications: Children 14 years or less; senile patients, history or symptoms of G.I. inflammation or ulceration including severe, recurrent or persistent dyspepsia; history or presence of drug allergy; blood dyscrasias; renal, hepatic or cardiac dysfunction; hypertension; thyroid disease; systemic edema; dermatitis and salivary gland enlargement due to the drug; polymyalgia rheumatica and temporal arteritis; patients receiving other potent chemotherapeutic agents, or long-term anticoagulant therapy.

Warnings: Age, weight, dosage, duration of therapy, existence of concomitant diseases, and concurrent potent therapy affect incidence of toxic reactions. Carefully instruct and observe the individual patient, especially the aging (forty years and over) who have increased susceptibility to the toxicity of the drug. Use the most effective dosage. Weigh initially unpredictable effects against potential risk of severe, even fatal, reactions. The disease condition itself is unaltered by the drug. Use with caution in first trimester of pregnancy

Butazolidin® alka Geigy

Each capsule contains:
100 mg. phenylbutazone USP
100 mg. dried aluminum hydroxide gel USP
150 mg. magnesium trisilicate USP

If it doesn't work in a week, forget it.

and in nursing mothers. Drug may appear in cord blood and breast milk. Serious, even fatal, blood dyscrasias, including aplastic anemia, may occur suddenly despite regular hemograms, and may become manifest days or weeks after cessation of drug. Any significant change in total white count, relative decrease in granulocytes, appearance of immature forms, or fall in hematocrit should signal immediate cessation of therapy and complete hematologic investigation. Unexplained bleeding involving CNS, adrenals, and G.I. tract has occurred. The drug may potentiate action of insulin, sulfonylurea, and sulfonamide-type agents. Carefully observe patients taking these agents. Nontoxic and toxic goiters and myxedema have been reported (the drug reduces iodine uptake by the thyroid). Blurred vision can be a significant toxic symptom worthy of a complete ophthalmologic examination. Swelling of ankles or face in patients under sixty may be prevented by reducing dosage. If edema occurs in patients over sixty, discontinue drug.

Precautions: The following should be accomplished at regular intervals: Careful detailed history for disease being treated and detection of earliest signs of adverse reactions; complete physical examination including check of patient's weight; complete weekly (especially for the aging) or an every two week blood check; pertinent laboratory studies. Caution patients about participating in activity requiring alertness and coordination, as driving a car, etc. Cases of leukemia have been reported in patients with a history of short- and long-term therapy. The majority of these patients were over forty. Remember that arthritic-type pains can be the presenting symptom of leukemia.

Adverse Reactions: This is a potent drug; its misuse can lead to serious results. Review detailed information before beginning therapy. Ulcerative esophagitis, acute

and reactivated gastric and duodenal ulcer with perforation and hemorrhage, ulceration and perforation of large bowel, occult G.I. bleeding with anemia, gastritis, epigastric pain, hematemesis, dyspepsia, nausea, vomiting and diarrhea, abdominal distention, agranulocytosis, aplastic anemia, hemolytic anemia, anemia due to blood loss including occult G.I. bleeding, thrombocytopenia, pancytopenia, leukemia, leukopenia, bone marrow depression, sodium and chloride retention, water retention and edema, plasma dilution, respiratory alkalosis, metabolic acidosis, fatal and nonfatal hepatitis (cholestasis may or may not be prominent), petechiae, purpura without thrombocytopenia, toxic pruritus, erythema nodosum, erythema multiforme, Stevens-Johnson syndrome, Lyell's syndrome (toxic necrotizing epidermolysis), exfoliative dermatitis, serum sickness, hypersensitivity angitis (polyarteritis), anaphylactic shock, urticaria, arthralgia, fever, rashes (all allergic reactions require prompt and permanent withdrawal of the drug), proteinuria, hematuria, oliguria, anuria, renal failure with azotemia, glomerulonephritis, acute tubular necrosis, nephrotic syndrome, bilateral renal cortical necrosis, renal stones, ureteral obstruction with uric acid crystals due to uricosuric action of drug, impaired renal function, cardiac decompensation, hypertension, pericarditis, diffuse interstitial myocarditis with muscle necrosis, plevascular granulomata, aggravation of temporal arteritis in patients with polymyalgia rheumatica, optic neuritis, blurred vision, retinal hemorrhage, toxic amblyopia, retinal detachment, hearing loss, hyperglycemia, thyroid hyperplasia, toxic goiter, association of hyperthyroidism and hypothyroidism (causal relationship not established), agitation, confusional states, lethargy; CNS reactions associated with overdosage, including convulsions, euphoria, psychosis, depression, headaches, hallucinations, giddiness, vertigo, coma, hyperventilation, insomnia; ulcerative stomatitis, salivary gland enlargement. (B)98-146-070-H(10/71)

For complete details, including dosage, please see full prescribing information

GEIGY Pharmaceuticals
Division of CIBA-GEIGY Corporation
Ardley, New York 10502

More than sleep.

your choice of sleep medication
is wisely based on more than
sleep-inducing potential

sleep with relative safety

Chronic tolerance studies have confirmed the relative safety of Dalmane (flurazepam HCl); no depression of cardiac or respiratory function was noted in patients administered recommended or higher doses for as long as 90 consecutive nights.

In most instances when adverse reactions were reported, they were mild, infrequent and seldom required discontinuance of therapy. Morning "hang-over" with Dalmane has been relatively infrequent. Dizziness, drowsiness, lightheadedness and the like have been the side effects noted most frequently, particularly in the elderly and debilitated. (An initial dose of Dalmane 15 mg should be prescribed for these patients.)

sleep for 7 to 8 hours
without need to
repeat dosage

No sleep medication has been as rigorously evaluated in the sleep research laboratory as Dalmane. Insomnia patients given one 30-mg capsule of Dalmane at bedtime, on average: fell asleep within 17 minutes, had fewer nighttime awakenings, spent less time awake after sleep onset, and slept for 7 to 8 hours with no need to repeat dosage during the night.

sleep with
consistency

Dalmane has been shown to be consistently effective even during consecutive nights of administration, with no need to increase dosage.

Dalmane (flurazepam HCl) is a distinctive sleep medication—a benzodiazepine specifically indicated for insomnia. It is not a barbiturate or methaqualone, nor is it related chemically to any other sedative hypnotic.

When your evaluation of insomnia indicates the need for a sleep medication, consider Dalmane—a single entity nonnarcotic, non-habit-forming agent proved effective and relatively safe for relief of insomnia.

DALMANE[®]

(flurazepam HCl)

When restful sleep is indicated

One 30-mg capsule h.s. —usual adult dosage
(15 mg may suffice in some patients)

One 15-mg capsule h.s. —initial dosage for elderly or debilitated patients.

Before prescribing Dalmane (flurazepam HCl), please consult Complete Product Information, a summary of which follows:

Indications: Effective in all types of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings and/or early morning awakening; in patients with recurring insomnia or poor sleeping habits; and in acute or chronic medical situations requiring restful sleep. Since insomnia is often transient and intermittent, prolonged administration is generally not necessary or recommended.

Contraindications: Known hypersensitivity to flurazepam HCl.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. Caution against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Use in women who are or may become pregnant only when potential benefits have been weighed against possible hazards. Not recommended for use in persons under 15 years of age. Though physical and psychological dependence have not been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage.

Precautions: In elderly and debilitated, initial dosage should be limited to 15 mg to preclude oversedation, dizziness and/or ataxia. If combined with other drugs having hypnotic or CNS-depressant effects, consider potential additive effects. Employ usual precautions in patients who are severely depressed, or with latent depression or suicidal tendencies. Periodic blood counts and liver and kidney function tests are advised during repeated therapy. Observe usual precautions in presence of impaired renal or hepatic function.

Adverse Reactions: Dizziness, drowsiness, lightheadedness, staggering, ataxia and falling have occurred, particularly in elderly or debilitated patients. Severe sedation, lethargy, disorientation and coma, probably indicative of drug intolerance or overdosage, have been reported. Also reported were headache, heartburn, upset stomach, nausea, vomiting, diarrhea, constipation, GI pain, nervousness, talkativeness, apprehension, irritability, weakness, palpitations, chest pains, body and joint pains and GU complaints. There have also been rare occurrences of sweating, flushes, difficulty in focusing, blurred vision, burning eyes, faintness, hypotension, shortness of breath, pruritus, skin rash, dry mouth, bitter taste, excessive salivation, anorexia, euphoria, depression, slurred speech, confusion, restlessness, hallucinations, and elevated SGOT, SGPT, total and direct bilirubins and alkaline phosphatase. Paradoxical reactions, e.g., excitement, stimulation and hyperactivity, have also been reported in rare instances.

Dosage: Individualize for maximum beneficial effect. *Adults:* 30 mg usual dosage; 15 mg may suffice in some patients. *Elderly or debilitated patients:* 15 mg initially until response is determined.

Supplied: Capsules containing 15 mg or 30 mg flurazepam HCl



ROCHE LABORATORIES
Div., Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

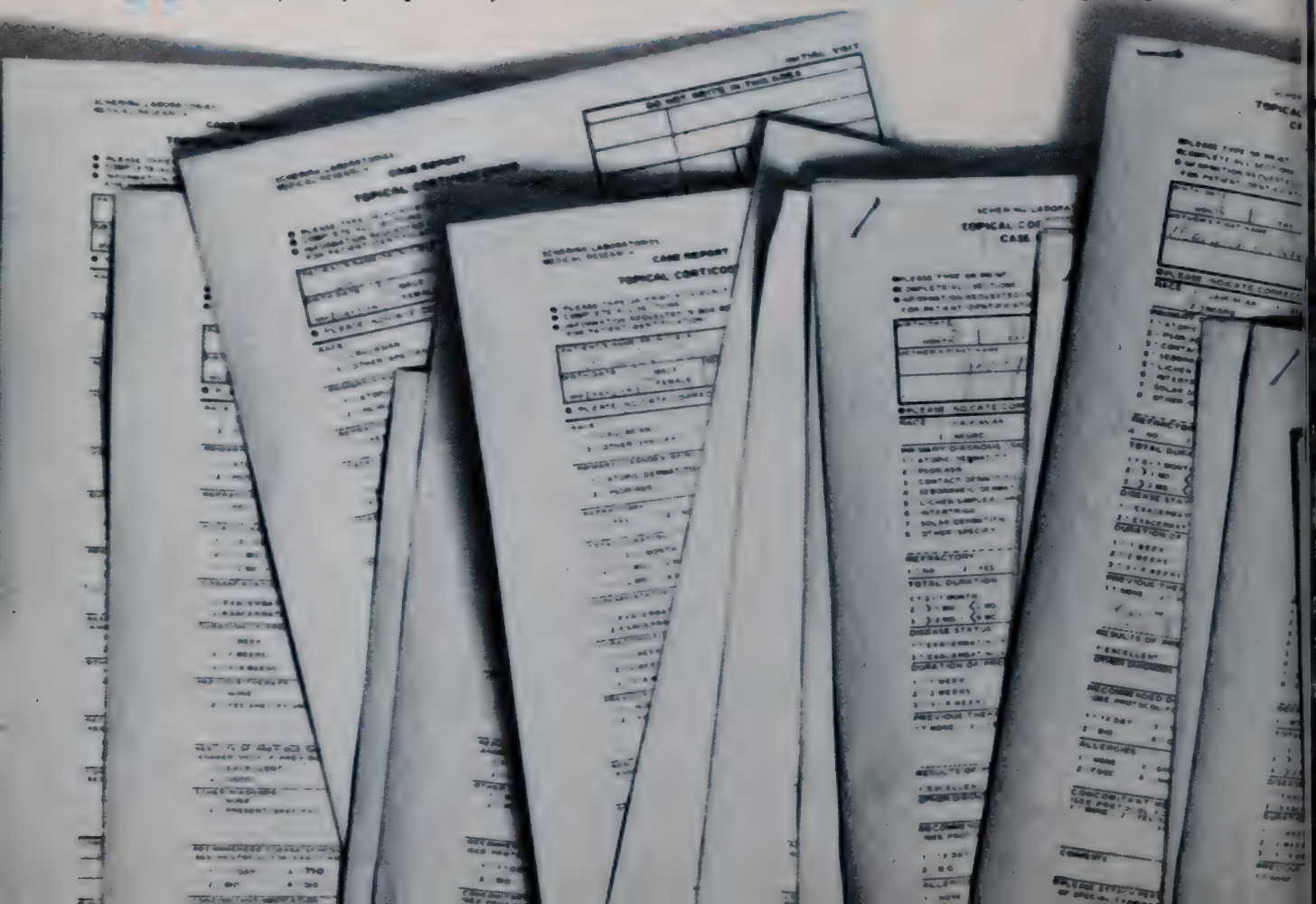
A topical steroid that has clinically succeeded

*in study...after study...after study*¹⁻⁶

Excellent/good results

85% in psoriasis
(150 of 177 patients)¹

92% in atopic eczema
(231 of 251 patients)¹





Valisone

brand of

betamethasone valerate (0.1%) Cream/Ointment

Plus economy B.i.d. dosage often found effective!
Available in 5, 15, and 45 Gm. tubes.

96% in contact dermatitis
(81 of 84 patients)¹

CLINICAL CONSIDERATIONS:

Description VALISONE products contain betamethasone valerate (9-fluoro-11 β ,17,21-trihydroxy-16 β -methylpregna-1,4-diene-3,20-dione 17-valerate). Each gram of VALISONE Cream 0.1% contains 1.2 mg. betamethasone valerate (equivalent to 1.0 mg. betamethasone) in a soft, white, hydrophilic cream of water, mineral oil, petrolatum, polyethylene glycol 1000 monocetyl ether, cetostearyl alcohol, monobasic sodium phosphate, and phosphoric acid; 4-chloro-m-cresol is present as a preservative. Each gram of VALISONE Ointment 0.1% contains 1.2 mg. betamethasone valerate (equivalent to 1.0 mg. betamethasone) in an ointment base of liquid and white petrolatum, and hydrogenated lanolin. VALISONE Cream and Ointment contain no parabens.

Indications VALISONE Cream and Ointment are indicated for the relief of the inflammatory manifestations of corticosteroid-responsive dermatoses.

Contraindications VALISONE Cream and Ointment are contraindicated in vaccinia and varicella. Topical steroids are contraindicated in those patients with a history of hypersensitivity to any of the components of the preparation.

Precautions If irritation develops with the use of VALISONE Cream or Ointment, treatment should be discontinued and appropriate therapy instituted. In the presence of an infection, the use of an appropriate antifungal or antibacterial agent should be instituted. If a favorable response does not occur promptly, the corticosteroid should be discontinued until the infection has been adequately controlled. If extensive areas are treated or if the occlusive technique is used, the possibility exists of increased systemic absorption of the corticosteroid and suitable precautions should be taken. Although topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use in pregnant females has not been absolutely established. Therefore, they should not be used extensively in pregnant patients, in large amounts, or for prolonged periods of time. VALISONE Cream and Ointment are not for ophthalmic use.

Adverse Reactions The following local adverse reactions have been reported with topical corticosteroids: burning, itching, irritation, dryness, folliculitis, hypertrichosis, acneiform eruptions, and hypopigmentation. The following may occur more frequently with occlusive dressings than without such therapy: maceration of the skin, secondary infection, skin atrophy, striae, and miliaria.

Dosage and Administration Apply a thin film of VALISONE Cream or Ointment to the affected skin areas one to three times a day. Clinical studies of VALISONE have indicated that dosage only once or twice a day is often feasible and effective. AUGUST 1972
For more complete details, consult Schering literature available from your Schering Representative or Professional Services Department, Schering Corporation, Kenilworth, New Jersey 07033.

References: (1) Files of Headquarters Medical Research Division, Schering Corporation. (2) Carter, V. H., and Noojin, R. O.: *Curr. Therap. Res.* 9:253, 1967. (3) Falk, M. S.: *Cutis* 2:788, 1966. (4) Goldblum, R. W.: *Pennsylvania Med.* 69:50, 1966. (5) Nieman, M. M.: *J. Indiana M. A.* 10:1184, 1966. (6) Zimmerman, E. H.: *Arch. Dermat.* 95:514, 1967.

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EDUCATION: H

OCCUPATION: D

RESIDENCE: E

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ROCHE announces new

BACTRIMTM

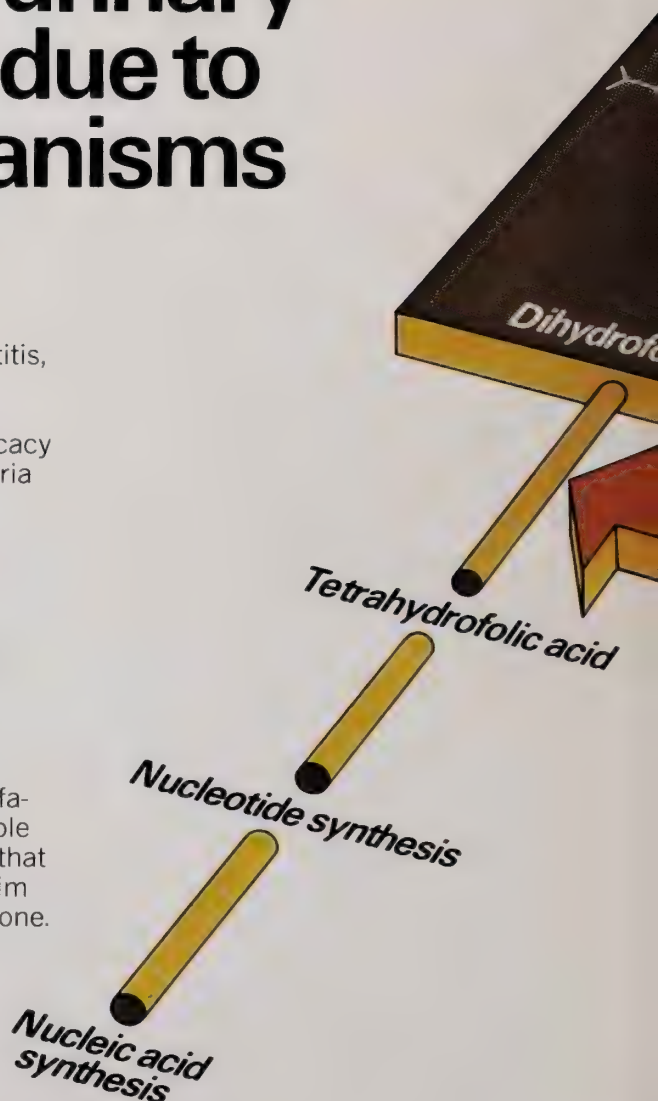
Each tablet contains 80 mg trimethoprim and 400 mg sulfamethoxazole.

a new type of antibacterial for a two-pronged attack against chronic urinary tract infections due to susceptible organisms

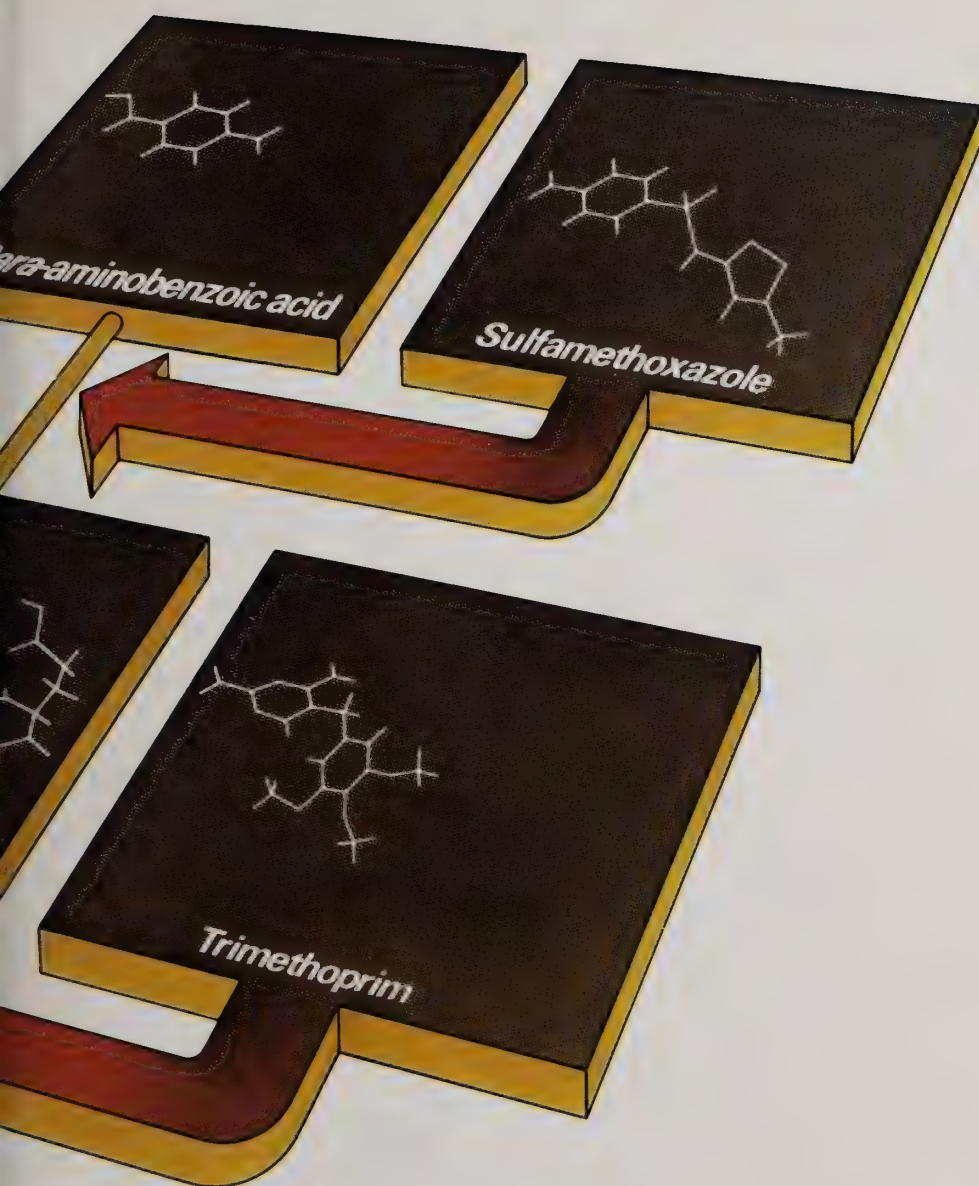
Bactrim is highly effective in the treatment of these infections—primarily pyelonephritis, pyelitis and cystitis, when due to susceptible organisms (usually *E. coli*, *Klebsiella-Enterobacter*, *Proteus mirabilis*, and, less frequently, indole-positive proteus species). This efficacy is related to the unique mode of action against bacteria (see opposite page), an action that, in effect, makes Bactrim a new type of antibacterial.

Bactrim significantly superior to constituents in patients with obstructive complications

In the presence of obstructive uropathy, Bactrim has demonstrated efficacy which is superior to either sulfamethoxazole or trimethoprim alone against susceptible organisms. In addition, *in vitro** studies have shown that bacterial resistance develops more slowly with Bactrim than with either trimethoprim or sulfamethoxazole alone.



*Please note that clinical conclusions cannot be extrapolated from *in vitro* studies.



Interrupts life cycle of susceptible bacteria

Unique mode of action interrupts the life cycle at two important points, thereby impeding the production of nucleic acids and proteins essential to these bacteria. These consecutive interruptions occur because sulfamethoxazole and trimethoprim resemble naturally existing substrates. By competitive replacement of these substrates, they inhibit further synthesis.

new **BACTRIMTM**

Each tablet contains 80 mg trimethoprim and 400 mg sulfamethoxazole.

for chronic urinary tract infections

Before prescribing, please see complete product information on last page of advertisement.

Excellent clinical response in chronic urinary tract infections

A multiclinic, double-blind study* of response to a ten-day course of therapy in 471† patients with chronic urinary tract infections demonstrated the superiority of Bactrim. On the 10th day after initiation of therapy, 91.7% (of 168 patients) showed significant bacteriological response to Bactrim compared with 81.2% (of 144 patients) to trimethoprim and 64.5% (of 155 patients) to sulfamethoxazole. In patients with obstructive complications, 10th day response was 94.8% (of 97 patients) to Bactrim, 72.9% (of 85 patients) to trimethoprim and 58.5% (of 94 patients) to sulfamethoxazole.

Excellent response maintained

Bactrim proved equally impressive in maintaining this bacteriological response. In the above study, after ten-day therapy with Bactrim, 68.4% of patients with chronic urinary tract infections maintained response for up to 42 consecutive days, compared with 59.7% with trimethoprim and 44.4% with sulfamethoxazole. In patients with obstruction, 70.8% of those on Bactrim maintained response for up to 42 consecutive days, compared

with 49.4% on trimethoprim and 38.8% on sulfamethoxazole. The figures are particularly remarkable in cases with urinary obstruction—cases regarded as being notoriously difficult to treat.

To date, low incidence of significant side effects

Although Bactrim demonstrated impressive clinical results, it is important to note that the incidence of clinically significant adverse effects was low, mainly nausea and/or vomiting, rash, leukopenia, SGOT increase and creatinine increase.

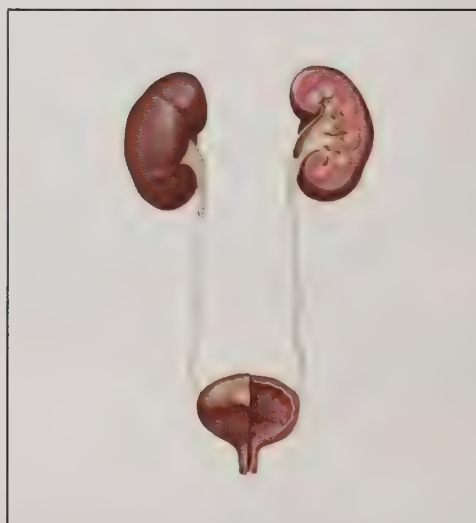
Bactrim should be given with caution to patients with impaired renal or hepatic function, possible folate deficiency and to those with severe allergy or bronchial asthma. Adequate fluid intake must be maintained. Complete blood counts, urinalyses with careful microscopic examination, and renal function tests should be performed during therapy.

Currently, the increasing frequency of resistant organisms is a limitation of the usefulness of all antibacterial agents, especially in the treatment of chronic and recurrent urinary tract infections.

Usual adult dosage: two tablets every twelve hours for 10 to 14 days; no loading dose required.

* Data on file, Hoffmann-La Roche Inc., Nutley, N.J. 07110

† 4 patients not available for evaluation at day 10.



new **BACTRIM**™

Each tablet contains 80 mg trimethoprim and 400 mg sulfamethoxazole.

for chronic urinary tract infections



Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, N.J. 07110

Before prescribing, please consult complete product information on facing page.

Complete Product Information:

Description: Bactrim is a synthetic antibacterial combination product, available in scored light-green tablets, each containing 80 mg trimethoprim and 400 mg sulfamethoxazole.

Trimethoprim is 2,4-diamino-5-(3,4,5-trimethoxybenzyl) pyrimidine. It is a white to light-yellow, odorless, bitter compound with a molecular weight of 290.3.

Sulfamethoxazole is N¹-(5-methyl-3-isoxazoly) sulfanilamide. It is an almost white in color, odorless, tasteless compound with a molecular weight of 253.28.

Actions: Microbiology: Sulfamethoxazole inhibits bacterial synthesis of dihydrofolic acid by competing with para-aminobenzoic acid. Trimethoprim blocks the production of tetrahydrofolic acid from dihydrofolic acid by binding to and reversibly inhibiting the required enzyme, dihydrofolate reductase. Thus, Bactrim blocks two consecutive steps in the biosynthesis of nucleic acids and proteins essential to many bacteria.

In vitro studies have shown that bacterial resistance develops more slowly with Bactrim than with trimethoprim or sulfamethoxazole alone.

In vitro serial dilution tests have shown that the spectrum of antibacterial activity of Bactrim includes the common urinary tract pathogens with the exception of *Pseudomonas aeruginosa*. The following organisms are usually susceptible: *Escherichia coli*, *Klebsiella-Enterobacter*, *Proteus mirabilis* and indole-positive proteus species.

Representative Minimum Inhibitory Concentration Values for Bactrim-Susceptible Organisms (MIC—mcg/ml)				
Bacteria	Trimethoprim alone	Sulfamethoxazole alone	TMP/SMX (1:20) TMP SMX	
<i>Escherichia coli</i>	0.05—1.5	1.0 —245	0.05—0.5	0.95— 9.5
<i>Proteus spp.</i> indole positive	0.5 —5.0	7.35 —300	0.05—1.5	0.95—28.5
<i>Proteus mirabilis</i>	0.5 —1.5	7.35 — 30	0.05—0.15	0.95— 2.85
<i>Klebsiella-Enterobacter</i>	0.15—5.0	0.735—245	0.05—1.5	0.95—28.5

Human Pharmacology: Bactrim is rapidly absorbed following oral administration. The blood levels of trimethoprim and sulfamethoxazole are similar to those achieved when each component is given alone. Peak blood levels for the individual components occur one to four hours after oral administration. The half-lives of sulfamethoxazole and trimethoprim, 10 and 16 hours respectively, are relatively the same regardless of whether these compounds are administered as individual components or as Bactrim. Detectable amounts of trimethoprim and sulfamethoxazole are present in the blood 24 hours after drug administration. Free sulfamethoxazole and trimethoprim blood levels are proportionately dose-dependent. On repeated administration, the steady-state ratio of trimethoprim to sulfamethoxazole levels in the blood is about 1:20.

Sulfamethoxazole exists in the blood as free, conjugated and protein-bound forms; trimethoprim is present as free, protein-bound and metabolized forms. The free forms are considered to be the therapeutically active forms. Approximately 44 percent of trimethoprim and 70 percent of sulfamethoxazole are protein-bound in the blood. The presence of 10 mg percent sulfamethoxazole in plasma decreases the protein binding of trimethoprim to an insignificant degree; trimethoprim does not influence the protein binding of sulfamethoxazole.

Excretion of Bactrim is chiefly by the kidneys through both glomerular filtration and tubular secretion. Urine concentrations of both sulfamethoxazole and trimethoprim are considerably higher than are the concentrations in the blood. When administered together as in Bactrim, neither sulfamethoxazole nor trimethoprim affects the urinary excretion pattern of the other.

Indications: Chronic urinary tract infections (primarily pyelonephritis, pyelitis and cystitis) due to susceptible organisms (usually *E. coli*, *Klebsiella-Enterobacter*, *Proteus mirabilis*, and, less frequently, indole-positive proteus species).

Important note: Currently, the increasing frequency of resistant organisms is a limitation of the usefulness of all antibacterial agents, especially in the treatment of chronic and recurrent urinary tract infections.

Contraindications: Hypersensitivity to trimethoprim or sulfonamides. Pregnancy and during the nursing period (see Reproduction Studies).

Warnings: Deaths associated with the administration of sulfonamides have been reported from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias. Experience with trimethoprim alone is much more limited, but it has been reported to interfere with hematopoiesis in occasional patients. In elderly patients concurrently receiving certain diuretics, primarily thiazides, an increased incidence of thrombopenia with purpura has been reported.

The presence of clinical signs such as sore throat, fever, pallor, purpura or jaundice may be early indications of serious blood disorders. Complete blood counts should be done frequently in patients receiving Bactrim. If a significant reduction in the count of any formed blood element is noted, Bactrim should be discontinued.

At the present time, there is insufficient clinical information on the use of Bactrim in infants and children under 12 years of age to recommend its use.

Precautions: Bactrim should be given with caution to patients with impaired renal or hepatic function, to those with possible folate deficiency and to those with severe allergy or bronchial asthma. In glucose-6-phosphate dehydrogenase-deficient individuals, hemolysis may occur. This reaction is frequently dose-related. Adequate fluid intake must be maintained in order to prevent crystalluria and stone formation. Urinalyses with careful microscopic examination and renal function tests should be performed during therapy, particularly for those patients with impaired renal function.

Adverse Reactions: For completeness, all major reactions to sulfonamides and to trimethoprim are included below, even though they may not have been reported with Bactrim.

Blood dyscrasias: Agranulocytosis, aplastic anemia, megaloblastic anemia, thrombopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia.

Allergic reactions: Erythema multiforme, Stevens-Johnson syndrome, generalized skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis.

Gastrointestinal reactions: Glossitis, stomatitis, nausea, emesis, abdominal pains, hepatitis, diarrhea and pancreatitis.

C.N.S. reactions: Headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo, insomnia, apathy, fatigue, muscle weakness and nervousness.

Miscellaneous reactions: Drug fever, chills, and toxic nephrosis with oliguria and anuria. Periarteritis nodosa and L. E. phenomenon have occurred.

The sulfonamides bear certain chemical similarities to some goitrogens, diuretics (acetazolamide and the thiazides) and oral hypoglycemic agents. Goiter production, diuresis and hypoglycemia have occurred rarely in patients receiving sulfonamides. Cross-sensitivity may exist with these agents. Rats appear to be especially susceptible to the goitrogenic effects of sulfonamides, and long-term administration has produced thyroid malignancies in the species.

Dosage and Administration: Not recommended for use in children under 12 years of age.

The usual adult dosage is two tablets every 12 hours for 10 to 14 days.

For patients with renal impairment:

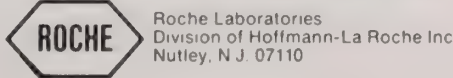
Creatinine Clearance (ml/min)	Recommended Dosage Regimen
Above 30	Usual standard regimen
15-30	2 tablets every 24 hours
Below 15	Use not recommended

How Supplied: Tablets, containing 80 mg trimethoprim and 400 mg sulfamethoxazole—bottles of 100 and 500; Tel-E-Dose® packages of 1000; Prescription Paks of 40, available singly and in trays of 10. Imprint on tablets: ROCHE 50.

Reproduction Studies: In rats, doses of 533 mg/kg sulfamethoxazole or 200 mg/kg trimethoprim produced teratological effects manifested mainly as cleft palates. The highest dose which did not cause cleft palates in rats was 512 mg/kg sulfamethoxazole or 192 mg/kg trimethoprim when administered separately. In two studies in rats, no teratology was observed when 512 mg/kg of sulfamethoxazole was used in combination with 128 mg/kg of trimethoprim. However, in one study, cleft palates were observed in one litter out of 9 when 355 mg/kg of sulfamethoxazole was used in combination with 88 mg/kg of trimethoprim.

In rabbits, trimethoprim administered by intubation from days 8 to 16 of pregnancy at dosages up to 500 mg/kg resulted in higher incidences of dead and resorbed fetuses, particularly at 500 mg/kg. However, there were no significant drug-related teratological effects.

BACTRIMTM
Each tablet contains 80 mg trimethoprim and 400 mg sulfamethoxazole.





**The Puerto Rico Medical Association
and
The Purdue Frederick Scientific Research**

AWARDS

**for Excellence in Presentation
of Original Scientific Research
by Medical Students,
Interns and Residents**

FIRST PRIZE \$300

SECOND PRIZE \$200

THIRD PRIZE \$100

Each prize will be accompanied by an engraved commemorative certificate.

The Purdue Frederick Company has long had an avid interest in the continuing research efforts of the medical profession, and now, to encourage significant competitive research among students, interns and residents, is pleased to announce an annual program of cash awards for the presentation of their original research at the

**Annual Meeting of the Puerto Rico Medical Association
to be held at San Juan Hotel
on Nov. 7-10, 1973.**

**The Scientific Committee of the
Puerto Rico Medical Association will select the winners,
who will be announced at the Annual Meeting.**

PREVALENCE OF INTESTINAL PARASITES IN A PUERTO RICAN COMMUNITY

Wilda B. Knight, MS

Dwayne Lee, Ph.D

Barnett L. Cline, MD

The prevalence of intestinal parasitic infection in Puerto Rico has been documented previously (1, 2, 3). These studies have been based on surveys of select population groups with narrow age limits, such as school children and military recruits. Virtually no information is available on the prevalence of parasitic infections in an entire community.

Our laboratory recently initiated a long-term community-based study of the natural history of *Schistosoma mansoni* in Parcelas de Boquerón, a rural community of about 1000 inhabitants in eastern Puerto Rico. While performing fecal examinations for *S. mansoni*, we also collected data for a descriptive study of the prevalence and intensity of infection with other intestinal parasites. This information provides a useful base line for evaluating the impact of future changes in the community.

Living standards in Puerto Rico have rapidly improved during the last decade. Higher living standards are reflected in Parcelas de Boquerón by the presence of electricity and running water in every home. Almost half of the homes have flush toilets and those without toilets have latrines. Most homes are constructed of concrete block, and the majority of families have one or more automobiles. A secondary objective of our study was to examine whether intestinal parasitism in the community reflected a generally improved standard of living, and whether within the community, risk and intensity of infection were related to housing conditions and type of sanitary facilities.

Materials and Methods

A house-to-house census was performed and information was obtained on age, sex, and occupation of residents, as well

Contribution of the San Juan Tropical Disease Laboratories, Ecological Investigations Program, Center for Disease Control, Health Services and Mental Health Administration, Public Health Service; U. S. Department of Health, Education, and Welfare, GPO Box 4532, San Juan, Puerto Rico 00936.

as type of construction and sanitary facilities for each house.

Ninety percent of the residents provided a single fecal specimen. One gram of each specimen was preserved in 10 percent formalin, and examined by the Ritchie formol-ether concentration technique (4). For helminth eggs and protozoan cysts, the following criteria were used to quantitate intensity of infection: 1+ for 1-10 eggs; 2+ for 11-100, 3+ for 101-300, 4+ for 301-500, 5+ for over 500 eggs per gram of stool.

In this study, hookworm refers to either *Ancylostoma duodenale* or to *Necator americanus*.

Results

The prevalence of parasitic infections by age group was determined (Figure 1). Trichuriasis was the most common infection, with an overall prevalence of 56 percent, reaching 80 percent in the 5-to-14-year age group. The distribution of density of egg excretion per gram of feces was as follows: 20 percent (1+); 55 percent (2+); 13 percent (3+); 5 percent (4+) and 7 percent (5+). Of 212 infected persons in the 5-to-14 age group, 11 percent excreted 500 eggs or more per gram of feces, as compared to 4.6 percent for the other age groups.

Eleven percent of the population harbored hookworms and the 15-to-19-year age group showed a peak prevalence of 26 percent. The distribution of density of egg excretion for hookworm was as follows: 23 percent (1+); 55 percent (2+); 15 percent (3+); 4 percent (4+) and 3 percent (5+).

FIGURE 1
RESULTS OF SINGLE STOOL EXAMINATIONS ON 907 PERSONS
PREVALENCE OF PARASITIC INFECTION BY AGE GROUP
PARCELAS DE BOQUERON, PUERTO RICO
NOV-DEC 1971

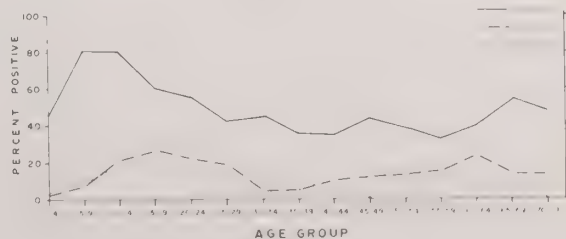


TABLE I: COMPARISON OF PREVALENCE OF PARASITIC INFECTION IN PERSONS WITH TOILET OR LATRINE IN THE HOME – PARCELAS DE BOQUERON, P. R. (1971)

Parasite	Number Tested	Persons Living in Homes with				Percent Positive
		TOILET			LATRINE	
		Number Positive	Percent Positive	Number Tested	Number Positive	
<i>T. trichiura</i>	423	181	43	474	293	62
<i>A. lumbricoides</i>	423	6	1	474	6	1
Hookworm	423	34	8	474	82	17

TABLE II: COMPARISON OF PREVALENCE OF PARASITIC INFECTIONS IN PERSONS LIVING IN HOMES CONSTRUCTED OF CONCRETE BLOCK OR WOOD AND CONCRETE – PARCELAS DE BOQUERON, PUERTO RICO (1971)

Parasite	Number Tested	Persons Living in Homes Constructed of				Percent Positive
		CONCRETE BLOCK		WOOD OR WOOD AND CONCRETE		
		Number Positive	Percent Positive	Number Tested	Number Positive	
<i>T. trichiura</i>	659	330	50	246	149	61
<i>A. lumbricoides</i>	659	6	1	246	6	2
Hookworm	659	66	10	246	49	20

Entamoeba coli was found in 11 percent of the population. The prevalence of *Ascaris lumbricoides*, *Strongyloides stercoralis*, and *Balantidium coli* was less than 2 percent.

The prevalence of parasitic infections in persons living in homes with toilets was compared with the prevalence in persons living in houses with latrines (Table I). The data indicate that persons living in homes with toilets were less commonly infected with *T. trichiura* and hookworm than persons living in homes with latrines. However, prevalence of infection with these parasites was high in both groups. Ascariasis was not common in either group (1 percent).

The prevalence of parasitic infection in persons living in concrete homes was compared with the prevalence in persons living in homes of wood or wood and cement

(Table II). Persons living in homes constructed of wood or wood and cement tended to have higher rates of trichuriasis and hookworm infection than persons living in concrete houses.

Discussion

The high prevalence of trichuriasis in the 5-to-9-year group (80 percent) was similar to the level (75 percent) reported previously in Puerto Rico for the comparable age group (3).

The low prevalence of ascariasis is somewhat surprising. Maldonado and Oliver González (1959) reported a prevalence of about 25 percent, and Greenberg and Ferguson (1971) found 13.4 percent of the population infected with ascariasis.

Parcelas de Boquerón has a high standard of living compared to typical impoverished rural communities, yet the prevalence of intestinal parasitism is relatively high. Our data suggest the need for community-based epidemiologic studies to examine in detail some of the factors which account for the persistence of intestinal parasites in a community such as Parcelas de Boquerón. It will be necessary to examine social and behavioral attributes of the population as well as environmental factors to gain a clear understanding of this problem.

Summary

The prevalence of intestinal parasites was studied in a 1,000-member community in eastern Puerto Rico. Trichuriasis was the most common helminth infection, with an overall prevalence of 56 percent. The prevalence of hookworm and *Entamoeba coli* infection was 11 percent. Ascariasis was found in 1 percent of the population. Persons living in homes with flush toilets had lower prevalences of parasitic infection than persons living in homes with latrines.

Resumen

La prevalencia de infección con parásitos intestinales fue estudiada en una comunidad de 1,000 habitantes,

localizada en el este de Puerto Rico. Trichuriasis fue la infección helmíntica más común, con una prevalencia de 56 por ciento. La prevalencia de uncinariasis y *Entamoeba coli* fue de 11 por ciento y la de Ascariasis 1 por ciento. La prevalencia parasítica fue más baja en los residentes de casas con inodoros que en los residentes de casas con letrinas.

Acknowledgments

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PROGRESO TERAPEUTICO

SEPTICEMIA Y SHOCK SEPTICO

Carlos H. Ramírez Ronda, MD

En la práctica diaria de la medicina nos encontramos muchas veces con el cuadro de septicemia y shock séptico. Se define septicemia como una enfermedad sistémica causada por la presencia de microorganismos o sus toxinas en la sangre y el síndrome de shock séptico resulta como consecuencia de estos microorganismos en el torrente sanguíneo, resultando en perfusión inadecuada de los tejidos. Finalmente se decompensa la circulación capilar debido a pobre perfusión; los tejidos y células sufren daño y puede llegarse a una etapa de daño irreversible.

Los organismos que causan mayormente bacteremia son los cocos gram positivos como *Diplococcus pneumoniae*, *Streptococcus* (varios) y los bacilos aeróbicos gram negativos como *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* y *Proteus mirabilis*. Un tercer grupo de microorganismos que está causando un gran número de episodios de bacteremia son las bacterias aneróbicas como *Bacteroides* y *Streptococcus anaerobius*. La bacteremia gram negativa es la causa más frecuente del síndrome de shock séptico en pacientes hospitalizados y es la causante de un gran número de muertes. Tiene una mortalidad de 50 por ciento. Usualmente se manifiesta en varones de más de cuarenta años, mas es frecuente también en mujeres jóvenes con abortos sépticos. Los factores que predisponen a septicemia y shock séptico en orden de importancia son, infecciones del tracto urinario, infecciones del tracto biliar, infecciones del tracto gastrointestinal, cirugía o manipulaciones quirúrgicas; cirrosis hepática, diabetes mellitus, cancer, leucemias, radioterapia, antimetabólitos, esteroides y transfusiones de sangre contaminada. La fuente más común de bacteremia son las vías urinarias. Para que ocurra el shock séptico la presencia de bacterias en la sangre no es necesaria ya que puede ocurrir debido a las endotoxinas bacterianas, invasión

directa bacteriana u oclusión del flujo sanguíneo a un órgano vital.

Se debe sospechar sepsis gram negativa y shock temprano, para tratar de prevenir complicaciones y evitar la alta mortalidad. En cualquier persona de edad madura que desarrolla fiebre, escalofríos e hipotensión se sospecha shock séptico. Las manifestaciones clínicas pueden variar, puede tener la piel tibia y seca, el pulso abundante y buen flujo urinario, en esta etapa se encuentra en la fase tibia de shock causada por la endotoxina liberada. No debe dejarse progresar a la etapa de shock franco donde hay palidez, sudoración, piel fría y húmeda, cianosis periferal, colapso de venas y un pulso débil y rápido que nos lleva a pobre perfusión y anuria.

En el shock séptico, vemos hipotensión que puede deberse a un déficit de volumen real, a fallo cardíaco o a un déficit de volumen funcional secundario a acumulación periferal de sangre. Si medimos la presión venosa central (PVC) notamos que cuando hay un déficit de volumen, la PVC está baja y el tratamiento se dirige a corregir este déficit. Si la PVC está elevada significa congestión y el tratamiento se dirige a aumentar la eficiencia de la bomba. Cuando existe un déficit de volumen funcional en donde la PVC está baja y se mantiene baja después de reemplazar coloides o cristaloideos se considera que existe fallo periferal vascular y se procede a corregirse.

Bacteremia lleva a un descenso inmediato de la PVC y la resistencia periferal como resultado compensador, el débito cardíaco aumenta, aunque el efecto neto es perfusión pobre. Concomitantemente se libera histamina y 5-hidroxitriptamina que causa dilatación arteriolar, mientras las vénulas permanecen contraídas; como resultado se acumula sangre periferalmente disminuyendo el retorno venoso; se disminuye el débito cardíaco y el defecto de perfusión empeora. Las endotoxinas pueden activar el sistema de coagulación y subsiguientemente el sistema fibrinolítico causando hemorragias y por consiguiente déficit intravascular mayor. Todo esto resulta en hipoxia tisular y acidosis láctica que puede resultar en un estado metabólico irreversible. Para tratar bien el paciente tenemos que parar este proceso

TABLA I: ESQUEMA DE MANEJO

I. Reconocimiento

A. Sospeche shock séptico

1. En un paciente de edad avanzada, con fiebre, escalofríos, que tenga infección urinaria o instrumentación reciente.
2. Mujer joven con aborto incompleto, fiebre y escalofríos.

B. Diagnostique shock séptico

Cuando el paciente desarrolla hipotensión, baja la producción de orina, desarrolla pulso débil, la piel se humedece y se pone fría.

II. Diagnóstico

A. Pruebas rutinarias CBC, urinalisis, creatinina sérica, tiempo protrombina, plaquetas, fibrinogeno, electrolitos.

B. Cultivos de:

1. Sangre-varios aeróbicos, anaeróbicos
2. Orina
3. Garganta

C. Radiografía de pecho

III. Tratamiento

A. Inserte sonda siloplástica para medir presión venosa central (PVC).

1. Verifique qué punta está en vena cava superior con radiografía de tórax si hay duda.
2. Mida PVC.

B. Si PVC está baja (5 cm. H₂O o menos)

1. Colides (plasma o sangre)
2. Cristaloides (normal salina) hasta que PVC esté entre 8-12 cm. H₂O.

C. Si PVC está alta o el paciente sigue en shock después del paso B.

1. Isoproterenol 1.0 mg. en 55 cc 5 por ciento dextrosa en agua, 1-2 microgramos por minuto.
2. Digoxin 1.0 mg. I.V si el paciente no está previamente digitalizado.

D. Si el paciente no responde al paso C y permanece hipotenso.

1. Metaraminol 100 mg. en 500 cc 5 por ciento dextrosa en agua para subir presión sistólica 35-40 mm de Hg.

E. Uso de corticosteroides

1. Succinato de hidrocortisona (Solu Corteff) 1.0 gm. endovenoso inmediatamente y 500 mg. cada 2 horas.
2. Succinato de metilprednisolona (Solu Medrol) - 30 mg./Kg. endovenoso puede repetirse en 4 horas.

F. Antibióticos

1. Gentamicina (Garamycin) 3-5 mg./Kg./24 horas dividido en 3 dosis endovenoso.
2. Ampicillin 8-12 gms./24 hrs. EV en o dosis cada 4 horas o
3. Cefalotina (Keflin) 8-12 gms./24 hrs., EV en 6 dosis cada 4 horas.
4. Si se sospecha Pseudomonas:
Carbencilina (Pyopen) 25-30 gms. EV en 6 dosis cada 4 horas.

G. Parametros a seguir:

1. Producción de orina por hora 30-50 cc/hora, si baja
 - a) Furosemida (Lasix) 40-60 mg. EV
 - b) Mannitol 25 gms. E.V.
2. Presión venosa central - mantener entre 8-12 cms. H₂O
3. Signos vitales
4. Balance electrolítico y ácido base
5. Función renal

H. Modificar dosificación de acuerdo a función renal

I. Nunca comience terapia de antibióticos sin cultivos adecuados.

dinámico y luego revertirlo.

Manejo

La mejor terapia es la prevención; debe evitarse el uso de sondas de tipo Foley, el mal uso de antibióticos, no se debe dejar una sonda siloplástica endovenosa por más de 48 horas, debe de descontaminarse cuidadosamente los respiradores y nebulizadores y usar agujas de mariposa cuando sea posible para administrar líquidos endovenosos.

El reconocimiento del shock séptico se basa en tener una gran sospecha en pacientes con condiciones predisponentes como son infecciones urinarias, manipulaciones del tracto genitourinario y abortos. Si el paciente después de un procedimiento arriba mencionado, desarrolla hipotensión y taquicardia se sospecha shock séptico y se comienza a investigar inmediatamente.

Si no lo prevenimos y lo reconocemos, lo primero a hacer es insertar una sonda para medir presión venosa central y estar seguro que la punta de la sonda siloplástica esté en la vena cava superior, tomando una radiografía de pecho si hay duda. Concomitantemente se cultiva garganta, orina y sangre (aeróbica y anaeróbicamente) además de cualquier otro lugar obvio de infección. Si la PVC está baja (5 cm. de agua o menos) se administran coloides como plasma y sangre si los hay a la mano o cristaloideos como solución de salina normal hasta que la PVC esté entre 8-12 cms. de agua. Con la administración de líquidos y corrección de la PVC un gran número de pacientes revierten a normotensión y mantienen un flujo urinario adecuado. Si la PVC está alta o el shock persiste a pesar de haber reemplazado volumen estamos bregando con un problema de fallo de bomba o fallo periferal. En este momento debe de usarse isoproterenol (Isuprel); 1.0 mg. en 500 cc de dextrosa al 5 por ciento en agua y se corre a una velocidad de 1-2 microgramos por minuto (0.5 - 1.0 cc por minuto) para mantener normotensión y una frecuencia cardíaca menor de 110 por minuto. Si el paciente no está digitalizado se digitaliza rápidamente con Digoxin 1.0 mg. IV y se repite otra dosis de 0.25 mg. a 0.50 mg. en 2-4 horas, luego se sigue la digitalización dependiendo de la respuesta clínica. Si el paciente se mantiene hipotenso debe considerarse el uso de vasopresores. Puede usarse Metaraminol (Aramina) 100 mg. en 500 cc dextrosa 5 por ciento en agua para aumentar la presión sistólica de 35 a 40 mm de mercurio con el único propósito de mantener perfusión periferal, pero no debe de usarse vasopresores

para mantener el paciente normotenso.

Una vez se sospecha shock séptico debe usarse corticosteroides. Succinato de hydrocortisona (Solu-Corteff) 1.0 gramo endovenoso (EV) inmediatamente y dar cada 24 horas de 2.0 a 6.0 gramos; *la dosis debe ser frecuente cada 2 horas o en infusión continua*. Puede usarse succinato de metilprednisolona (SoluMedrol) 30 mg./Kg. intravenoso y repetirse en 4 horas. Experimentalmente se ha usado clorpromazina, (Torazina) fenoxibenzamina (dibenzilina) y pentolamina pero no se recomiendan para uso clínico.

Una vez se sacan los cultivos de sangre, orina, garganta y otro lugar obvio de infección se comienza terapia con antibióticos. Se comienza con gentamicina de 3-5 mg./kg./24 horas dividido en tres dosis endovenosas, conjuntamente se comienza con ampicilina 100-160 mg./kg./24 horas dividido en 6 dosis cada 4 horas. En sustitución de ampicilina puede usarse cefalotina (Keflin) en una dosis similar. Si se sospecha una infección con Pseudomonas debe usarse la combinación de gentamicina con carbenicilina. La dosis de carbenicilina es de 25-30 gramos por 24 horas, endovenoso dividido en seis dosis cada 4 horas. Esta misma combinación se recomienda para los pacientes con leucemia, linfomas y agranulocitosis con septicemia o sospecha de sepsis.

Mientras el paciente está bajo tratamiento, hay ciertos parametros a seguir para el manejo completo. Esto incluye medir el flujo urinario cada hora y debe mantenerse un flujo de 30-50 cc por hora para lo cual se necesita una sonda de tipo Foley usualmente. Si el flujo urinario es menor de 30-50 cc/hora debe de usarse Furosemina (Lasix) 40-60 mg. IV o Mannitol 25 gms. I.V. siempre y cuando la PVC esté normal. Deben seguirse los signos vitales, presión venosa central y flujo de orina cada hora. Los defectos electrolíticos deben corregirse y mantener el balance ácido base. La función renal del paciente en shock puede estar afectada, razón que motiva a medir con frecuencia la creatinina sérica y la depuración de creatinina. Las dosis de medicamentos deben ajustarse apropiadamente dependiendo de la función renal. No nos podemos olvidar que estamos usando agentes nefrotóxicos como gentamicina y que la función renal puede deteriorarse debido a estos factores.

En resumen se ha presentado la manera de reconocer, diagnosticar y tratar a los pacientes con el shock séptico y septicemia.

Reconocimiento

Quiero expresar mi agradecimiento al Dr. Mario R. García

Palmieri por revisar el manuscrito, su ayuda, consejo y estímulo y al Dr. Norman Maldonado por revisar y corregir el manuscrito y por sus sugerencias valiosas.

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INTRAHEPATIC CHOLESTASIS DUE TO ALPHA-METHYLDOPA: A CASE REPORT

José M. Torres Gómez, MD, FACP, FACC

Although the pathogenesis of intrahepatic cholestasis is still, to a certain extent, hypothetical, damage to the hepatocytic bile secretory apparatus is the mechanism most commonly accepted today (1). The alterations that lead to the disturbance of biliary secretion of the micelles of bile salts may be initiated by physical or metabolic agents. Among these agents, drugs such as chlorpromazine and methyl testosterone not uncommonly cause this type of jaundice (2). Not infrequently, causal relationship has been established between alpha-methyldopa and isolated abnormal liver function tests, positive direct Coombs reactions, and to a less extent, various degrees of hemolytic anemia. Rarely, however, has alpha-methyldopa been seen associated with the complete clinical and laboratory picture of intrahepatic cholestasis. The purpose of this article is to present such a case.

Case History

A 43-year old white gravida 5 para 3 married female (S. C.) was enrolled in a double-blind study where the therapeutic effectiveness of alpha-methyldopa and prazosin hydrochloride in the treatment of hypertension were to be compared. The patient had an episode of painless jaundice at the age of 10 years which lasted several days but which did not exhibit any other manifestations to indicate the presence of a serious illness. It did not recur even during her pregnancies although she became hyperglycemic in those occasions. Preeclampsia was diagnosed in her third pregnancy. About four years prior to the study she was told to have hypertension but was never treated with drugs. She followed a low salt diet initially but soon discontinued it. She used oral contraceptives in 1972 but had discontinued them four months prior to the time when she started to take alpha-methyldopa. She denied ever having any surgical or other medical disease.

On January 3, 1973 treatment was started. According to the protocol of the study, she was classified as a non-responder on February 28. On this day, the seal on the bottle was broken and it showed that she had fallen in the alpha-methyldopa group. She had been receiving 250 mg t.i.d. The dose was then increased to 250 mg q.i.d. She had been followed on a weekly-visit program and had felt very well up to March 13 at which time her skin began to itch. By the 16th the itching

became generalized and so intense that Benadryl (50 mg) had to be prescribed. There was not much relief. Since alpha-methyldopa was the *only* drug that the patient had been receiving, she was told to discontinue it. She received the last dose in the morning of the 17th. By the 18th she had noticed slight repugnance to foods, a dark color in her urine and a whitish appearance of her stools. She came to my office on the 19th. A mild icteric tint was apparent in her conjunctivae. Aside from the scratches on the skin, there were no other abnormal physical findings.

She was hospitalized on the 21st (Doctors Hospital). 50 mg of Benadryl were given orally on this and the following day (March 22) as treatment for her itching though by this time it had decreased considerably. On this day (22nd), the conjunctivae already appeared normal and the urine had almost returned to its normal color. Her feces were normal on the 23rd, and from the 24th on, all of her symptoms and signs had disappeared. She has remained asymptomatic since then. She never had fever, hepatomegaly, splenomegaly, or right upper quadrant abdominal pain or tenderness.

Laboratory Results (See Tables I and II)

The first noticeable change that alerted us to the reaction that was developing, occurred on February 27 when an SGOT (glutamic transaminase) of 159 units was reported. By this time, the patient had received 41 grams of alpha-methyldopa in 55 days. By March 20, when the clinical picture of cholestasis was already evident, serum bilirubin, alkaline phosphatase, lactic dehydrogenase (LDH) and cholesterol were all elevated. The SGOT had risen to 950 units. The Coombs test, that had been negative on three previous occasions, was now weakly positive. Two days later it became clearly positive. On March 20, the serum haptoglobin was low indicating that hemolysis had taken place although the hemoglobin values remained more or less unchanged. Fractionation (isoenzymes) of LDH showed evidence of hepatic involvement. The test for the Australia antigen in the serum was negative. There were no significant alterations in the white blood cell counts and eosinophilia was not observed.

Within one week after withdrawal of the drug, the patient became completely asymptomatic. Two days later (March 26), the laboratory results had reverted to practically normal values with the exception of the

TABLE I

Date	Hemat. Percent	Hemog. Gms	WBC	Neutro Percent	Lymph. Percent	Eosin. Percent	Coombs (Direct)	Urine (Bile)
11/10/72	39	13.8	6096	54	43	3	neg.	
1/3/73	Alpha-methyldopa started (250 mg t.i.d.)							
1/5/73	37	12.3	5538	67	31	2 (Baso)	neg.	
2/27/73	39	13.6	5998	69	31	0	neg.	
3/17/73	Alpha-methyldopa discontinued.							
3/20/73	40	13.7	4426	59	39	2	pos. (weakly)	pos.
3/22/73	Serum Haptoglobin - 20 mg (low).						pos.	
3/25/73	Australian antigen ¹²⁵ in serum - negative.							
3/26/73	41	14.4	5866	62	37	1 (Mono)	neg.	
4/11/73	37.1	12.5	6912	69	31	0	neg.	

TABLE II

Date	S. Bilir.	Alk.Phos.	SGOT	LDH	Choles	T.Prot.	Albu.	Gluko
11/10/72	0.41	30	40	190	177	7.4	5.8	110
1/3/73	Alpha-methyldopa started (250 mg t.i.d.)							
1/5/73	0.32	29	4	165	182	7.4	5.07	102
2/27/73	0.42	26	159	203	169	7.58	5.08	107
3/17/73	Alpha-methyldopa discontinued.							
3/20/73	1.84	77	950	350	263	7.59	4.45	108
3/21/73	LDH fractionation (isoenzymes) - increased liver fraction.							
3/24/73			520 (SGPT)					
3/26/73	0.84	54	348	225	179	7.33	4.72	
4/11/73	0.69	50	30	168	206	7.27	4.8	111

SGOT. However, even this transaminase showed a marked reduction in activity (950 to 348 units). By April 11, all the laboratory tests were normal.

Discussion

In medicine, it is always difficult to prove, beyond any doubt, that an agent is responsible for a given syndrome. Sometimes, though the requisites demanded are not satisfied, enough events are so interrelated that one can arrive at a valid conclusion. I believe that such is the case at hand. The absence of parente-

ral medication, dental care, vaccination and other contacts do not give support to the diagnosis of viral hepatitis. The rapid and complete disappearance of both clinical and laboratory abnormalities as soon as the drug was withdrawn favors a direct relationship between alpha-methyldopa and the hepatic syndrome that had developed. The low value for haptoglobin and the changing reaction of the Coombs test indicate that we were dealing with a known reaction to this drug at that time. Though it would have been convenient to know the results of a needle biopsy of the liver, it was not carried out because of the patient's

rapid recovery. At any rate, it is doubtful that it would have helped to establish an etiological diagnosis since the hepatic reaction produced by alpha-methyldopa looks like viral hepatitis. In fact, histologically, the hepatic reaction to this drug is composed, in nearly equal proportions, of hepatitis and cholestasis (3). The negativity of the test for Australia (hepatitis-associated) antigen makes unlikely the postulate that the drug may have activated the virus thus making the disease coincidental with viral hepatitis (4). Moreover, tests for this antigen have been negative in drug-related jaundice (5). It is obvious, however, that this does not rule out Type I or A hepatitis as a possible etiology.

There are only two ways (not available as yet) in which we could have arrived at a specific diagnosis. One is through a test for recognition of viral hepatitis as such, and the other is through an immunologic test for recognition of the alpha-methyldopa reaction (3). Until these two tests are developed, we have to continue to make our judgments on the basis of what we have at hand. A third way in which we could have obtained more support for our diagnosis would have been through the process of challenging the patient with the drug again. However, since the patient was somewhat reluctant to this suggestion, since complete recovery from a second reaction could not be guaranteed, and since a negative reaction would not of necessity prove that the first one was not drug-related, it was decided not to carry out the challenge. In this case, the information obtained and the order in which events occurred lead us to the diagnosis of intrahepatic cholestasis due to alpha-methyldopa rather than to viral hepatitis with cholestasis.

Summary

A case of intrahepatic cholestasis supported by clinical and laboratory evidence is presented. About 1 1/2 months after taking alpha-methyldopa (only drug ingested), the SGOT became elevated. Itching was the initial symptom. It became intense in the presence of a very modest elevation of the serum bilirubin. The entire clinical picture returned to normal within a week of drug-withdrawal. The case is presented as one of

intrahepatic cholestasis secondary to alpha-methyldopa with the purpose to make our physicians aware of this reaction, since this drug is being increasingly used in the treatment of hypertension. Complete recovery following the withdrawal of the drug is the rule.

Resumen

Se presenta un caso de colestasis intrahepática. La transaminasa glutámica oxaloacética aumentó después de la paciente haber tomado alfa-metildopa por mes y medio. La enferma no tomó ninguna otra droga. El síntoma inicial fue picor el cual se volvió intenso en la presencia de una modesta elevación de la bilirrubina sérica. El cuadro clínico completo desapareció a la semana de haberse discontinuado la droga. Se presenta este caso como uno de colestasis intrahepática debido a alfa-metildopa con la intención de alertar a nuestros médicos sobre esta reacción ya que esta droga se está usando cada vez más en el tratamiento de la hipertensión. Lo usual es que se obtenga una recuperación total al discontinuarse la droga.

Acknowledgment

Dr. Walter Cervoni was responsible for all the laboratory studies performed in this case with the exception of the determination of haptoglobin and the test for the Australia antigen which were done at the Veterans Administration Hospital through the courtesy of Dr. Rodrigo Menéndez Corrada.

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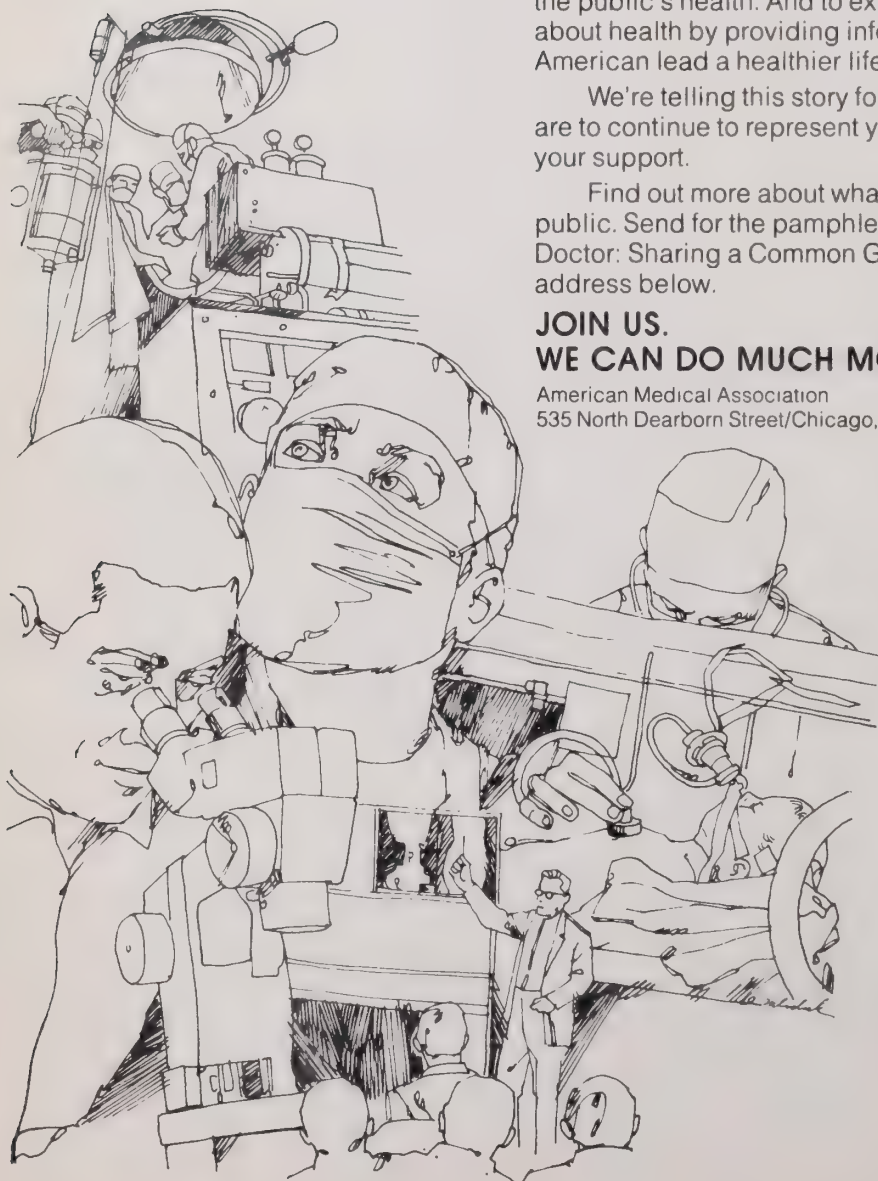
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AUSENCIA CONGENITA DE LOS MUSCULOS ABDOMINALES — “PRUNE BELLY”: REPORTE DE UN CASO

Luis C. Nina Ortega, MD

Todos, o casi todos los músculos abdominales pueden estar ausentes al nacer. En ocasiones solo un lado del abdomen está afectado, faltando uno o más grupos musculares.

Hasta el año 1971, 165 casos han sido reportados en la literatura. Ausencia sub-total o total de la musculatura abdominal es encontrada con mayor frecuencia que las ausencias localizadas.

Paciente

Récord número 07-19-04

Fecha de nacimiento: 11-5-72

Lugar de nacimiento: Centro de Salud de Lajas. Admitido en el Centro Médico de Mayagüez el 11-5-72 a las tres horas de nacido.

Historia materna y familiar: Edad de la madre: 26 años. Número de embarazos: grava V - Para V. Los otros cuatro hijos son normales. Tipo sanguíneo. O+. No consanguinidad entre los esposos. Otros familiares son normales. Enfermedades durante el embarazo: anemia hipocrómica (tratada con hierro parenteral al final del embarazo). Complicaciones del embarazo: ninguna.

Informaciones del parto: Duración de gestación: 40 semanas. Cuidado prenatal: Sí. Trabajo del parto: normal, 1er. estadio - 15-30ms. 2do. estadio - 15ms. Bolsas de las aguas rotas artificialmente. Presentación: Vx. Posición: L.O.A. Parto: vaginal. Infante al nacer fue dado un apgar score de: 1er. m-8 5m - 9.

Examen físico: Bebé a término con un llanto débil. Color normal excepto por acrocyanosis. Peso al nacer: 3.686 gms. (8.2 lbs). Circunferencia cefálica: 35cms. CT-34cms. L-48cms. Circunferencia abdominal: 49cms. Temp. 36.0° c. Hallazgos positivos: Torax aparece relativamente corto (ligemente desplazado hacia arriba). Surco sub-costal profundo. Inspección abdomen: Asimétrico. Asas intestinales “dibujadas” debajo de la piel. Un abultamiento generalizado abdominal era evidente, con mayores prominencias notadas en los flancos e hipocondrios. La piel era arrugada en toda su área abdominal (prune belly) y caía pesadamente lateralmente y hacia abajo. Palpación: Asas intestinales fueron

fácilmente palpadas al igual que los riñones. No había dolor al palparse libremente todo el abdomen flácido en todas sus áreas. El resto del examen físico fue normal.

Investigación:

1. Examen radiológico: I. V. P. mostró ureteroectasia marcada en el lado derecho. Otras áreas urinaria fue apreciada normal.
2. Laboratorio: Hb- 20gms - Hct 62 por ciento - WBC 11,080 cm^3 - Seg. 52 por ciento - L-44 por ciento - EOS 2 por ciento - B - 2 por ciento.
3. Chest X Ray - normal

Discusión

No hay una predisposición hereditaria en esta condición. Varones predominan entre los afectados en todas las series reportadas. La musculatura abdominal deriva del segmento muscular embrionario original por un proceso que envuelve su división en epímero e hipómero. Este último crece ventralmente hasta rodear la cavidad abdominal, fusionarse con los diferentes segmentos y dividirse en varias capas.

Todo este proceso embriológico se inicia en la quinta semana y es completado a las doce semanas cuando el defecto abdominal anterior es finalmente cerrado por fusión de los músculos rectos abdominales. Un fallo del desarrollo muscular abdominal debe ser provocado por algún daño al embrión durante el segundo mes de gestación.

Este desorden se asocia con relativa frecuencia a otros defectos congénitos, principalmente del tracto genito-urinario, por ejemplo: hidroureter e hidronefrosis, múltiples quistes renales, ausencia de gónadas o simplemente no descendidas. Otros defectos reportados son: vejiga urinaria muy distendida, anomalía de los pies, ano imperforado, etc.

Estos infantes pueden estar moribundos al nacer y morir en un período de una o dos horas. Otros menos seriamente afectados no parecen tan enfermos al nacer. El abdomen usualmente protrude grotescamente y cae pesadamente hacia los lados del abdomen haciéndose manifiesto la ausencia de soporte muscular abdominal. La piel está arrugada y su apariencia recuerda la de una ciruela por lo que este tipo de abdomen se le conoce

Del Departamento del Nursery, Centro Médico de Mayagüez, Puerto Rico.

como "PRUNE BELLY". Aquellos infantes que sobreviven el período neonatal están generalmente condenados por meses o años a padecer de pielonefritis crónica y una muerte temprana por uremia. El tratamiento de esta condición es solo de carácter paliativo, recomendándose el uso de una banda firme rodeando el abdomen. Esta medida parece mejorar el tono de la pared abdominal después de transcurrido algunos años. Reconstrucción quirúrgica es imposible debido a la escasez de tejido muscular en esta área.

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CATECHOLAMINES

The entire May, 1973 (Vol. 29, No. 2) issue of the British Medical Bulletin consists of a symposium entitled, "Catecholamines" (c), under the authorship of an international (mainly Great Britain) group of authorities. The symposium consists of 17 articles (including an introductory editorial-type paper), the majority of which are of a basic science nature. Such topics discussed consist of the following: histochemical visualization and mapping (by immunofluorescence microscopy, etc.) of c.-containing pathways and storage sites in the brain and peripheral neurones, and their modification by psychoactive drugs; dopamine (DA) in invertebrates, with the comment on the interesting role of DA in the hardening and tanning of insect cuticles and eliciting of fire-fly phosphorescence; DA receptors and DA as a synaptic transmitter; detailed descriptions and diagrams of c. biosynthesis and catebolism, and biochemical aspects of monamine oxidase which exists in multiple mitochondrial forms; mechanisms and life history of norepinephrine and its release and uptake from sympathetic nerves (including smooth muscle uptake), and the effects of stimulation, drugs, chemicals, etc. on its release and uptake; the antagonistic interactions of prostaglandins of the E series with c. at adrenergic nerve-endings; adrenergic receptors- classification and properties, were discussed as a basis for their use in clinical medicine, as well as the clinical status of the controversial B-receptor subtypes; the mechanisms of action of antihypertensive drugs were reviewed, emphasizing the central adrenergic mechanism of certain drugs in hypertension; the functional aspects of c. in the CNS.

Clinical papers discussed the fruits of c. research in the form of antihypertensive drugs (history of drug therapy, value, side-effects and results of therapy);

the presently popular and increasingly important place of specific B-adrenoceptor blocking drugs in common cardiac disorders (angina pectoris, myocardial infarction and arrhythmias); and the physiology of DA in basal ganglia (striatum) function and disease (decreased in Parkinsonism), including drugs that augment or diminish dopaminergic activity, and the exciting implications of L-DOPA (a precursor of DA) as replacement therapy in Parkinson's Disease. Inter-relationships of nigro-striatal neurones, emotional stress, drugs used in schizophrenia, and other bodily functions were provocatively mentioned. Severe hypertension in patients treated with MAO inhibitors who ingest foods containing high tyramine content was again emphasized. Low plasma DA B-hydroxylase levels have been noted in familial dysautonomia.

The articles are each well-endowed with bibliographies.

This symposium reveals how basic science has contributed to advances in the everyday care of patients and hints to applications in other afflictions of mankind. It may be of interest and value to basic scientists, biochemists, pharmacologists and clinicians who want to know more about the underlying basis of drugs and diseases encountered almost daily.

The copy sells for \$6.50 and may be obtained from the British Medical Bulletin, 97 and 99 Park St., London, W1Y 4HQ.

For the interested, another symposium on catecholamines appeared recently in California Medicine 117: 32-62, Sept., 1972.

Charles D. Johnson, MD

VASO-DILATADORES Y SHOCK

Mientras nuevas drogas, antibióticos y sustitutos sanguíneos, han alterado significativamente la incidencia y mortalidad del shock hemorrágico, el shock debido a bacterias y endotoxinas aumenta, y su mortalidad asciende a más de 60 por ciento. El shock presenta todavía un problema de gran importancia en la práctica médica.

Quizás, de todos los avances que han ocurrido en esta área, el cambio radical en su definición conceptual ha sido el más importante. Por más de 50 años persistió una definición fisiológica con su concepto central de una tensión arterial reducida. El confundir un parámetro clínico con etiología explica por qué fue orientado el tratamiento por muchos años hacia restaurar la tensión arterial con vasopresores naturales o sintéticos. Fueron Lillehei, Nickerson, y Dietzman quienes gradualmente cambiaron este concepto, generando una intensa investigación a nivel microvascular, celular, y molecular y cambiando el concepto central a uno bioquímico.

Hoy día consideramos el defecto fundamental del shock como perfusión inadecuada a nivel celular, sea por defecto en la bomba cardíaca, en el volumen de perfusión, en la interacción de la microcirculación pre y post-capilar, o en el efecto directo de toxinas en las propias células. En el concepto unitario propuesto por Dietzman el efecto final es el mismo, e incluye una estimulación intensa del sistema simpático, una falla en la microcirculación, y eventualmente un defecto en la bomba y en el volumen. Como resultado, el débito cardíaco usualmente disminuye a pesar de la intensa vasoconstricción y estimulación simpática que ocurre siempre.

Al cambiar conceptualmente nuestra definición de shock hemos de orientar tratamiento hacia una mejor perfusión de la célula. Simultáneamente, debemos corregir la causa primaria de la condición, mejorar el volumen circulante, mejorar la contracción de la bomba, y restablecer el balance ácido-base necesario. Ahora nos movemos en dirección opuesta, y la vasoconstricción excesiva en shock se considera como factor dañino y mortal. De ahí surge la nueva tendencia al uso de vasodilatadores cuando antes enfatizábamos vasoconstrictores.

Obviamente, en el manejo del síndrome de shock no existe una droga mágica o solución específica. Consiste, como se apunta tan clara y completamente en el artículo sobre este tema por el Dr. Ramírez Ronda, de una gran suspicacia, una intuición diagnóstica aguda, y un abordaje sistemático que corrija los distintos desequilibrios encontrados. Es probable que las reglas generales y específicas que el Dr. Ramírez Ronda indica para el manejo del shock séptico se apliquen a los otros tipos de shock también. El principio general de expandir el volumen a un límite máximo, de mejorar el funcionamiento del músculo cardíaco, de corregir los procesos infecciosos ocurrentes, y de constantemente supervisar al paciente son principios generales aplicables a todos los tipos de shock, y serán exitosos especialmente en las etapas tempranas.

Pero, ¿cómo tratamos al paciente que presenta ya un cuadro de shock desarrollado y tardío y que no responde a las maniobras iniciales? Aquí aplica el uso de medicamentos vasoactivos. Quizás isoprotenerol es el más aceptable, porque en adición a su efecto inotrópico sobre el músculo cardíaco disminuye la vasoconstricción al producir una estimulación beta. Mejora el débito cardíaco y también la distribución de la sangre hacia los órganos vitales. El uso del digitalis es importante por su efecto salubre cardíaco, y que en adición prevenga la posible insuficiencia cardíaca resultante de la infusión de líquidos. El uso rutinario de la furosemida (Lasix) en dosis altas es valiosísimo pues no tan solo

resulta en efecto diurésico a nivel de los tubos renales, sino en la distribución de la sangre intra-renal, aumentando la perfusión cortical y disminuyendo el daño isquémico.

El uso de vasodilatadores ha sido recomendado por innumerables investigadores: el isoprotenerol, los esteroides y el clorpromacina tienen uso rutinario, pero la fenoxibenzamina (Dibencilina) está aprobada tan sólo para uso experimental. El isoprotenerol está limitado por la existencia o aparición de taquicardia. La clorpromacina es un agente vasodilatador efectivo pero su desventaja principal es el efecto depresor en las funciones cerebrales y hepáticas.

Los glucocorticoides benefician al paciente como sigue: disminuyen la resistencia periférica, aumentan la perfusión tisular, aumentan el retorno venoso, y ejercen un efecto inotrópico positivo en el corazón. En adición a esto, reducen el derrame de enzimas hidrolíticas potentes de los lisosomas de las células, lo cual es particularmente importante en la célula anóxica y acidótica. Conviene recordar que la acción vasodilatadora de los esteroides depende de la dosis, y que su eficacia aparece sólo en dosis masivas equivalentes a 2 a 6 gramos de hidrocortisona, o 30 mg/kg de metilprednisolona. Todo paciente que reciba vasodilatadores debe recibir también infusión concomitante de líquidos.

En pacientes resucitados con éxito de shock prolongado aparecen con frecuencia lesiones pulmonares severas. Investigación en este campo, en particular por Wilson, demostró edema, cambios en la membrana de la célula del alveolo, cambios en los granulocitos, y eventualmente hemorragias, todos aparentemente iniciados por la vasoconstricción pulmonar. El rol de la célula polimorfonuclear en las génesis del cuadro parece ser importante. Esta secuencia de cambios produce clínicamente un cuadro de insuficiencia pulmonar progresiva. En una serie de experimentos completos y elegantes, Wilson demostró el rol de los esteroides, específicamente succinato de metilprednisolona, para evitar estos cambios a nivel de la microcirculación. Es probable que esta protección resulte del efecto vasodilatador de esta sustancia y de su propiedad estabilizadora de lisosomas. Conviene apuntar que la presencia del anión succinato aparentemente es imprescindible para esta acción.

Un apunte final sobre el uso de vasoconstrictores: surge la posibilidad de algunas situaciones excepcionales en las cuales sea deseable aprovechar el efecto inotrópico excelente de la mayoría de las drogas vasoconstrictoras. Conviene, sin embargo, recordar siempre que la indicación para su uso es el efecto inotrópico cardíaco y no su efecto vasoconstrictor periférico, por ser este último un efecto indeseable y dañino. Se enfatiza la brevedad del uso del vasoconstrictor, y que siempre sea acompañado de un vasodilatador para contrarrestar los efectos secundarios nocivos.

Eduardo A. Santiago Delpín, MD, MS

SOBRE LA INCIDENCIA DE PARASITOSIS EN PUERTO RICO

En esta edición del Boletín se ha publicado un artículo sobre la incidencia de parasitosis que aún prevalece en una comunidad en el este de Puerto Rico. El artículo no señala nada que nos sorprenda, ya que Maldonado y Oliver-González (1) descubrieron una situación muy similar en una muestra mucho más amplia reportada por primera vez en el 1959 y subsiguientemente por Maldonado (2), en 1967 donde se demostraba que en 10 años aún había una alta incidencia de parasitosis en los lugares estudiados. No nos sorprende que en aquellos lugares donde haya mejores facilidades higiénicas y donde las construcciones sean de hormigón, indicando una mejor situación económica y educativa, haya una incidencia menor de parasitosis. Somos un país tropical donde la parasitosis es endémica y es mi opinión que continuará en algún grado a pesar de los programas de las autoridades de salud

por erradicarla. Es halagador ver como la incidencia de ascariasis ha disminuído en el estudio reportado.

Los autores no mencionan las condiciones de salud de los examinados. Igualmente, el estado nutricional resulta ser un aspecto de mucha importancia en este tipo de estudio y los autores no hacen comentarios sobre el particular. Es bien sabido que en el Puerto Rico de ayer la parasitosis coexistía íntimamente con la malabsorción o *esprú tropical* y consecuentemente la mala nutrición. Al igual que la parasitosis, la malabsorción en Puerto Rico, se ha descrito en niños y adultos de todas las edades. Es de interés que en otros lugares del Caribe como Jamaica y la República Dominicana el *esprú tropical* sea extremadamente raro o no existente (3). En el 1971 Fernández y colaboradores (4) reportaron un estudio amplio y científico en varias comunidades de la isla y apenas encontraron evidencia de mala nutrición.

En 1972 Klipstein y colaboradores (5) reportaron sus estudios del estado nutricional y la función intestinal en una comunidad rural de Bayamón. Noventa y seis adultos fueron seleccionados científicamente y evaluados cuidadosamente en el Centro de Investigaciones Clínicas de la Escuela de Medicina. Unas 46 personas o sea el 47 por ciento tenían parasitosis y unas 43 o sea 44 por ciento tenían alguna malabsorción o evidencia de anormalidad en el intestino delgado. Lo interesante de este estudio es que a pesar de estos hallazgos la inmensa mayoría de estas personas estaban asintomáticas y no tenían evidencia de deficiencia nutricional. Se atribuye ésto a que la nutrición de estos sujetos era adecuada. La ingestión de proteínas era mayor de 50 gramos al día en el 75 por ciento de los estudiados y aún en aquellas personas en que era menor, ésto no hizo diferencia en las pruebas de absorción.

Señalo

Señalo estos estudios para enfatizar el hecho que ni la parasitosis, ni la malabsorción han desaparecido de la isla. Mejores condiciones ambientales y una mejor nutrición han sido factores importantes en mantener clínicamente saludables cerca de un 50 por ciento de nuestros adultos y quizás un por ciento mayor de niños que padecen de parasitosis y malabsorción subclínica. En estos días de aumento en el costo de la vida y especialmente en los alimentos más nutritivos como la carne, leche, huevos, etc. hay que estar alerta a que nuestros ciudadanos de menos ingresos, especialmente los niños y ancianos no sean víctimas de las enfermedades con las que coexistimos. El discontinuar los alimentos federales a los necesitados para sustituirlos por un plan de sellos de alimentos, también debe ser observado cuidadosamente por nuestros nutricionistas para que no se revierta a patrones alimenticios que promueven la pérdida de la salud y el retorno al ayer casi olvidado.

En el mes de septiembre se celebra el centenario del natalicio del Dr. Bailey K. Ashford quien fuera pionero en la investigación y el tratamiento de la parasitosis, malabsorción y mala nutrición en Puerto Rico. A él le debemos muchos de los adelantos científicos en nuestra isla.

Norman Maldonado, M.D.

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NOTICIAS

AMERICAN LUNG ASSOCIATION (formerly N.T.R.D.A.) FELLOWSHIPS AND ASOCIACION PUERTORRIQUEÑA ANTITUBERCULOSA Y DE SALUD RESPIRATORIA

Fellowships in the field of lung disease are being offered by the former National Tuberculosis and Respiratory Disease Association which, effective May 20, 1973, changed its name to American Lung Association.

Training Fellowships directed toward a career in lung disease are offered to physicians entering their second or later year of residency in internal medicine, pediatrics, thoracic surgery, or other specialties, including basic sciences as related to lung disease; to candidates holding the degree of M.D., Ph.D., or Sc.D. for further training as scientific investigators in this field; and to graduate students who are to work on a research project and who have been admitted to candidacy for Ph.D. degree. The Fellowships will range in amount up to \$10,000 and will cover a one year period, with renewals possible for a maximum of three years' support. Applicants must be U. S. or Canadian citizens or foreign nationals holding permanent visas. Priority will be given to applicants interested in academic careers.

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Applications must be submitted by October 1. Address inquiries to: American Lung Association, Medical Director, 1740 Broadway, New York, N. Y. 10019.

HARDENING OF THE ARTERIES MAY BEGIN IN EARLY CHILDHOOD

CHICAGO — Atherosclerosis, or hardening of the arteries, sometimes begins in early childhood, and doctors caring for small children and adolescents are advised to make regular tests in an article in the Aug. 6th issue of the *Journal of the American Medical Association*.

The study reported in the article involved blood cholesterol tests in more than 2,000 normal children over a period of two years in Scottsdale, Arizona. From 10 to 35 percent were found to have an excess of cholesterol. Children in the study ranged in age from 2 weeks to 19 years.

If the physician discovers a high cholesterol count in a young patient, he can then advise the parents as to changes in diet to keep the condition under control.

Atherosclerosis means an accumulation of fatty substance inside the lining of the arteries. It leads to heart attacks. This build up can be retarded by a diet that is low in saturated fats.

The report is by Glenn Friedman, M. D., and Stanley J. Goldberg, M. D., of the University of Arizona College of Medicine, Tucson. It describes a simple test that can be performed in a physician's office to determine blood cholesterol level. It also offers a chart of average levels for various age groups, so that the physician can determine whether his patient is above the norm.

Cholesterol levels were found to increase with age.

ENZYMES FOUND TO GIVE ACCURATE ACCOUNT OF HEART ATTACK SEVERITY

CHICAGO — Just how severe was the heart attack that sent the patient to the hospital in great pain?

Determining the extent of damage to the heart in the early stage always has been difficult. But it is highly important in being able to predict the future of the patients and in determining the degree of therapy administered.

A Philadelphia physician reports in the Aug. 6th issue of the *Journal of the American Medical Association* that he has determined that measurements of the body's enzymes give an accurate picture of the severity of the heart attack.

In a study of 125 patients with acute myocardial infarction (heart attack), Eugene L. Coodley, MD, found a direct relationship between enzyme rise and early death.

Enzyme levels six times normal were found in more than half of the patients who died shortly after heart attacks.

Outward features of a heart attack often provide a rough indication of the severity of the attack, but these may be misleading, says Dr. Coodley. Electrocardiographic changes also are helpful, but sometimes are difficult to interpret. The usual laboratory tests are imprecise.

The value of enzyme determination in detection of heart attacks has been known for some years. The new study analyzes this in depth.

"In patients with documented myocardial infarction, the amplitude of enzyme rise was closely correlated with the various complications of myocardial infarction.

"The ability to predict complications in myocardial infarction may have important ramifications. More aggressive therapy might be indicated at an earlier stage in patients showing markedly elevated enzyme levels," Dr. Coodley says.

MEDICAL BRIEFS

A pacemaker, as most people know, is an electrical device, implanted in a heart patient to regulate his heart beat. Now, Canadian physicians have devised a pacemaker to straighten the spine. It is designed to, hopefully, correct the curved spine condition known as scoliosis, which affects mainly young girls. The spinal pacemaker sends out impulses which put the muscles controlling the vertebrae into intermittent spasms, forcing them into normal alignment, said Dr. Walter

Bobechko of the Hospital for Sick Children in Toronto. The device has been tested successfully in animals.

Scientists at the National Institutes of Health have found a way to grow living animal cells to a density resembling natural body tissue. Current methods allow many types of human and animal cells to be grown in the laboratory, but they stop growing at concentrations much lower than that of tissue. The new method uses an "artificial circulatory network," similar to blood vessels which supplies continuous nourishment. The scientists plan to use the technique to study cancer. By altering hormones and other ingredients in the fluid that feeds the cells, they will study conditions which promote or retard the growth of various kinds of cancer tissue.

It has long been known that many of those parents who abuse their children were themselves abused and neglected. Could the friendship of a motherly type help such parents break the abuse syndrome? St. Luke's Hospital in New York City recently announced it would try to find out in a new program.

Integument!

Our skin—the human integument—covers us, defines us, protects us. But skin is subject to cuts, burns, abrasions. And infections. Neosporin Ointment fights infection by providing broad antibacterial action against susceptible skin invaders. It contains antibiotics that are rarely used systemically, reducing the risk of sensitization.



INDICATIONS: *Therapeutically*, used as an adjunct to appropriate systemic therapy for topical infections, primary or secondary, due to susceptible organisms, as in:

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- primary pyodermas (impetigo, ecthyma, sycosis vulgaris, paronychia)
- secondarily infected dermatoses (eczema, herpes, and seborrheic dermatitis)
- traumatic lesions, inflamed or suppurating as a result of bacterial infection.

Prophylactically, the ointment may be used to prevent bacterial contamination in burns, skin grafts, incisions, and other clean lesions. For abrasions, minor cuts and wounds accidentally incurred, its use may prevent the development of infection and permit wound healing.

CONTRAINDICATIONS: Not for use in the external ear canal if the eardrum is perforated. This product is contraindicated in those individuals who have shown hypersensitivity to any of the components.

PRECAUTION: As with other antibiotic preparations, prolonged use may result in overgrowth of nonsusceptible organisms and/or fungi. Appropriate measures should be taken if this occurs. Articles in the current medical literature indicate an increase in the prevalence of persons allergic to neomycin. The possibility of such a reaction should be borne in mind.

Complete literature available on request from Professional Services Dept. PML.

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(POLYMYXIN B-BACITRACIN-NEOMYCIN)

Each gram contains: Aerosporin[®] brand Polymyxin B Sulfate 5,000 units; zinc bacitracin 400 units; neomycin sulfate 5 mg. (equivalent to 3.5 mg. neomycin base); special white petrolatum q.s. In tubes of 1 oz. and ½ oz. and ⅓ oz. (approx.) foil packets.



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Julian Katz, M.D.
*Assistant Professor of
Medicine and Director,
Clinical Research Laboratory,
Section of Gastroenterology,
Medical College of Pennsylvania*

Gastrin: an updated look at an important hormone

Early in this century Edkins showed that the intravenous injection of an extract of antral mucosa would stimulate gastric acid secretion. He gave the name gastrin to this proposed hormone. After Komarov substantiated the presence of such a hormone, Gregory and fellow workers isolated, characterized, and synthesized the polypeptide. Gastrin not only has an important influence on acid secretion, but also plays a major role in other gastrointestinal functions.

Structure

Antral gastrin contains 17 amino acids. It is remarkable that a 4 amino acid segment, the carboxyl terminal portion, can reproduce all the activities of which the whole molecule is capable.

Gastrin and feedback mechanism of acid secretion

Gastrin is produced primarily by the mucosal cells in the gastric antrum, the distal non-acid secreting portion of the stomach. The hormone stimulates the parietal cells in the fundus and body of the stomach to produce acid, and a negative feedback mechanism is initiated. Acid bathing the antrum acts directly on the gastrin-producing cell to inhibit release of the hormone.

Gastrin and the lower esophageal sphincter

Contraction of the gastroesophageal sphincter is stimulated by

gastrin. The sphincter muscle is more sensitive to the effects of gastrin than adjacent esophageal muscle. The efficacy of antacid therapy in reflux esophagitis may be due, in part, to the release of antral gastrin. Antacids neutralize gastric acid and raise the pH in the antrum. The gastrin which is then released increases the strength of the sphincter, which acts as a barrier against reflux.

Some other actions of gastrin

Beyond gastrin's prime role as a stimulator of gastric acid production, gastrin also acts on other parts of the G.I. tract. On the stomach, to stimulate (albeit weakly) pepsin production and increase gastric antral motility. On the pancreas, by stimulating enzyme secretion. On the liver, by increasing the flow of bile. On the intestine, by inhibiting absorption of water and electrolytes, and—possibly—increasing motility. And, on the ileocecal sphincter, by relaxing it (contrary to its action on the gastroesophageal sphincter), and perhaps contributing to the gastro-colic reflex.

Excessive gastrin production

It would be expected that if the stomach could not produce acid, gastrin release would continue unabated. Indeed such is the case in pernicious anemia, where there is achlorhydria, and circulating gastrin levels are very high. Alka-

linization of the antrum, vagal stimulation, and mechanical distension of the antrum all provoke gastrin release.

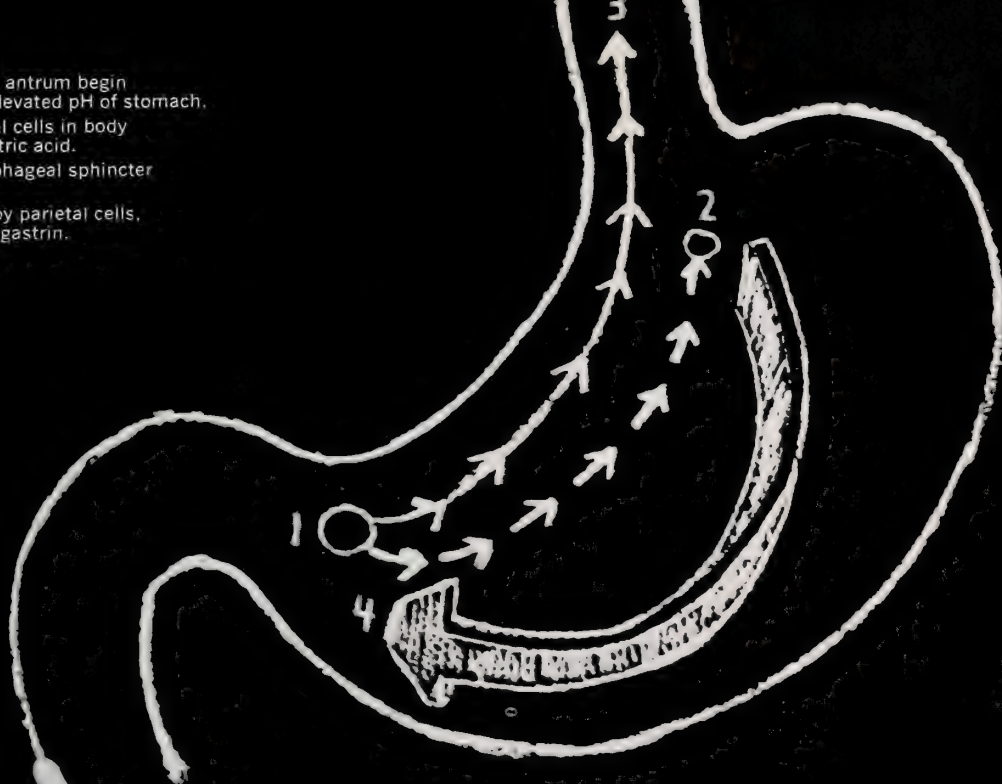
In the Zollinger-Ellison syndrome the radioimmunoassay of gastrin may be the best diagnostic technique. The islet-cell tumor produces large amounts of gastrin, leading to gastric hypersecretion and often intractable ulcer disease. Another situation in which gastrin levels may be high, is when the antrum is retained after gastric resection. Here the antrum is removed from the inhibitory effects of acid, and hypersecretion of gastrin occurs.

Some therapeutic implications

Obviously surgical removal of the antrum will lower gastric secretion as therapy for peptic ulcer disease. But other ways of antagonizing gastrin are being investigated. Some substances have a close structural similarity to the gastrin molecule. For example, cholecystokinin, the intestinal hormone, and caerulein, a material extracted from the skin of amphibians, contain in their structure a sequence of amino acids identical to the active terminal portion of gastrin. These substances are competitive inhibitors of gastric secretion. They combine with the receptor site for acid secretion, cause little stimulation of the receptor, and thus occlude the site.

Keys

1. Gastrin-producing cells in antrum begin secreting in response to elevated pH of stomach.
2. Gastrin stimulates parietal cells in body and fundus to secrete gastric acid.
3. Contraction of gastroesophageal sphincter facilitated by gastrin.
4. Resulting HCl, produced by parietal cells, inhibits further release of gastrin.



CamaloxTM: The pleasant answer to unpleasant problems of hyperacidity

Ever since Camalox was introduced, physicians have been making the discovery that here, indeed, is an antacid that does what an antacid is designed to do.

And does it most agreeably.

It neutralizes excess acid—associated with peptic ulcer, gastritis, esophagitis, hiatal hernia and heartburn.

Fast. And thoroughly.

Consider the patient suffering from hiatal hernia, with accompanying esophageal reflux—it is postulated that the release of gastrin during antacid alkalization of gastric contents may help the gastroesophageal sphincter constrict, thereby helping to stop reflux and subsequent heartburn.

There's something else: Non-constipating Camalox, with its balanced formulation made by a special process*, is smooth, non-gritty. These qualities, together with its refreshing vanilla-mint flavor, make it easy to take. The first time. Or the hundredth.

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Next time you've got a patient with hyperacidity, prescribe Camalox.

It's the pleasant answer...to an unpleasant condition.

Composition: Balanced formulation of magnesium and aluminum hydroxides with calcium carbonate.

Indications: As an antacid in the treatment and management of peptic ulcer, gastritis, gastric hyperacidity, hiatal hernia, peptic esophagitis, heartburn, indigestion, and upset stomach.

Warning: Camalox should not be used in patients who are severely debilitated or suffering from kidney failure.

Supplied: Camalox Tablets—bottles of 50 tablets and boxes of 100 tablets (in foil strips). Camalox Suspension—white liquid in convenient 12 fluid ounce plastic bottles and economical 16 ounce (pint) bottles.

*Patent pending.

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with calcium carbonate

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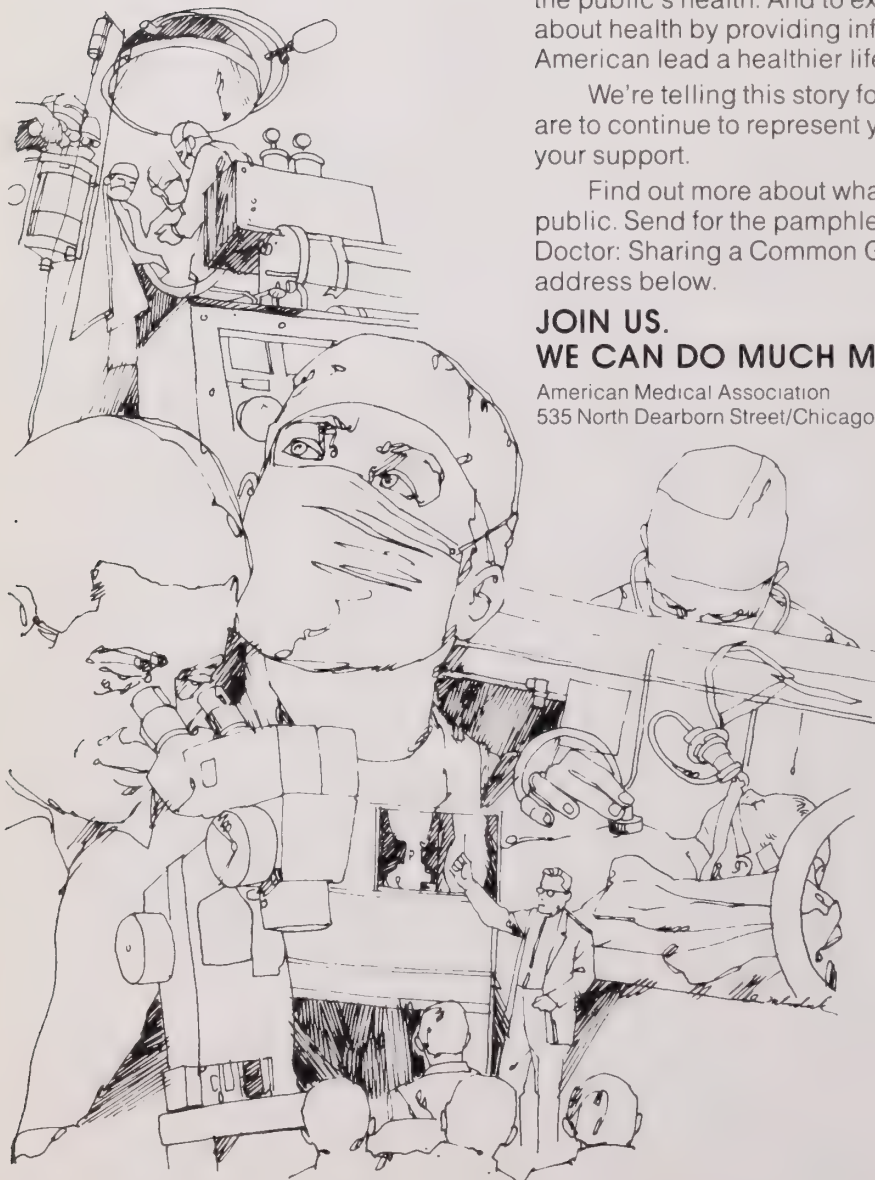
Perhaps you've seen pages in newspapers and national magazines signed "America's Doctors of Medicine." They're part of this program. It tells the true story of what it takes to become a doctor. The ways American medicine has improved the public's health. And to express the profession's concern about health by providing information which will help every American lead a healthier life.

We're telling this story for you, the American doctor. If we are to continue to represent you effectively, we need your support.

Find out more about what the AMA does for you and the public. Send for the pamphlet, "The AMA and the American Doctor: Sharing a Common Goal." Write: Dept. DW, at the address below.

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LA MAS FACIL DE LEER Y DE INTERPRETAR**

GRAVINDEX

Marca de Fábrica

LA PRUEBA EN LAMINA DE 3 MINUTOS QUE DETECTA EL EMBARAZO



ORTHO DIAGNOSTICS

Raritan, New Jersey 08869 E. U. A.

the bare facts.

in many dermatoses* the less they wear,
the more they need...

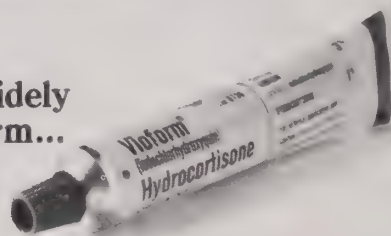
Vioform[®]-Hydrocortisone (iodochlorhydroxyquin and hydrocortisone)

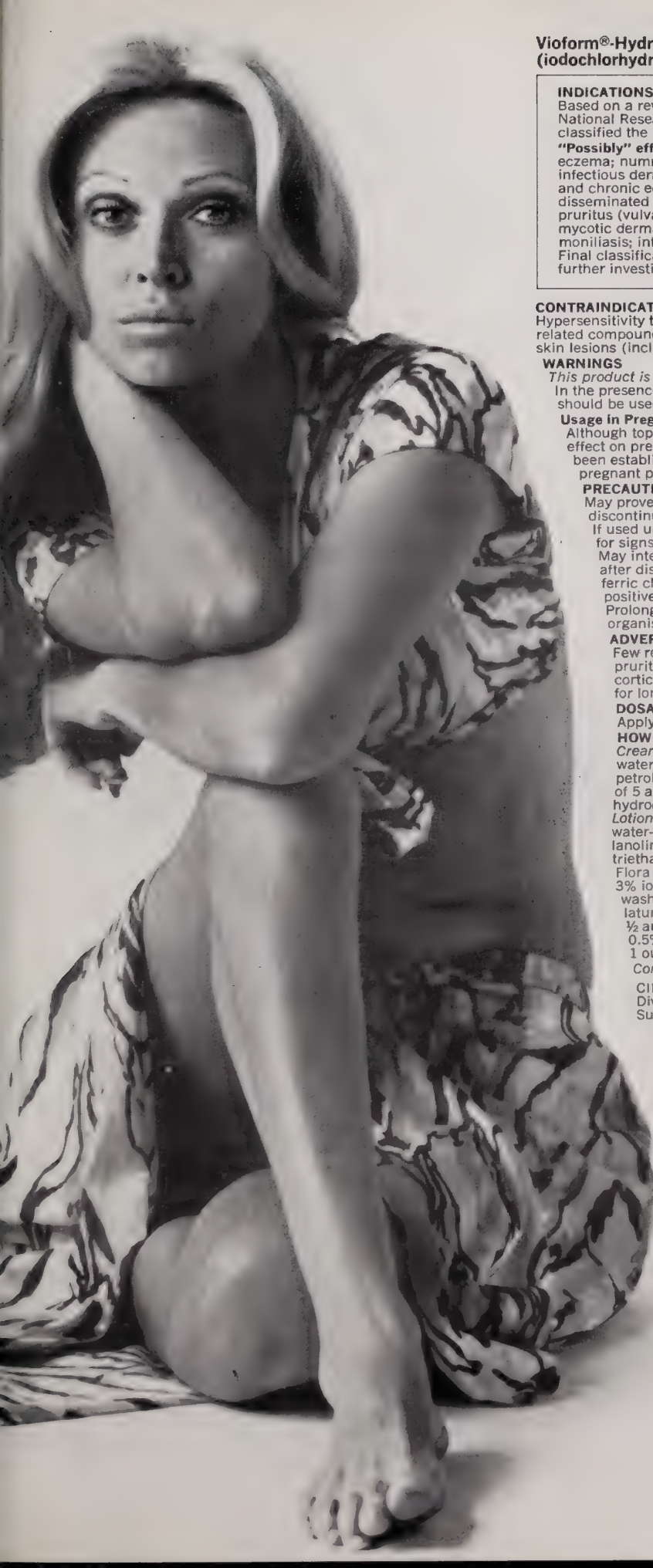
antifungal • antibacterial • anti-inflammatory • antipruritic

Some styles don't leave much to the imagination. And don't provide much cover for common dermatoses, either. Just like plain topical steroids. If the lesion has become infected with fungi or bacteria, plain topical steroids are ordinarily not recommended as sole therapy. Vioform-Hydrocortisone, on the other hand, provides the kind of comprehensive therapy these dermatoses may require. It not only supplies the anti-inflammatory and antipruritic actions of hydrocortisone...but also adds the antibacterial and antifungal actions of Vioform.

*This drug has been evaluated as possibly effective for these indications. See brief prescribing information.

**Another fact...
the most widely
prescribed form...
20 Gm cream**





Vioform®-Hydrocortisone
(iodochlorhydroxyquin and hydrocortisone)

INDICATIONS

Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, FDA has classified the indications as follows:

"Possibly" effective: Contact or atopic dermatitis; impetiginized eczema; nummular eczema; infantile eczema; endogenous chronic infectious dermatitis; stasis dermatitis; pyoderma; nuchal eczema and chronic eczematoid otitis externa; acne urticata; localized or disseminated neurodermatitis; lichen simplex chronicus; anogenital pruritus (vulvae, scroti, ani); folliculitis; bacterial dermatoses; mycotic dermatoses such as tinea (capitis, cruris, corporis, pedis); moniliasis; intertrigo.

Final classification of the less-than-effective indications requires further investigation.

CONTRAINDICATIONS

Hypersensitivity to Vioform-Hydrocortisone, or any of its ingredients or related compounds; lesions of the eye; tuberculosis of the skin; most viral skin lesions (including herpes simplex, vaccinia, and varicella).

WARNINGS

This product is not for ophthalmic use.

In the presence of systemic infections, appropriate systemic antibiotics should be used.

Usage in Pregnancy

Although topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use in pregnant females has not been established. Therefore, they should not be used extensively on pregnant patients in large amounts or for prolonged periods of time.

PRECAUTIONS

May prove irritating to sensitized skin in rare cases. If this occurs, discontinue therapy. May stain.

If used under occlusive dressings or for a prolonged period, watch for signs of pituitary-adrenal axis suppression.

May interfere with thyroid function tests. Wait at least one month after discontinuance of therapy before performing these tests. The ferric chloride test for phenylketonuria (PKU) can yield a false-positive result if Vioform is present in the diaper or urine.

Prolonged use may result in overgrowth of nonsusceptible organisms requiring appropriate therapy.

ADVERSE REACTIONS

Few reports include: Hypersensitivity, local burning, irritation, pruritus. Discontinue if untoward reaction occurs. Rarely, topical corticosteroids may cause striae at site of application when used for long periods in intertriginous areas.

DOSAGE

Apply a thin layer to affected areas 3 or 4 times daily.

HOW SUPPLIED

Cream, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearyl alcohol, spermaceti, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of 5 and 20 Gm. *Ointment*, 3% iodochlorhydroxyquin and 1% hydrocortisone in a petrolatum base; tubes of 5 and 20 Gm. *Lotion*, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearic acid, cetyl alcohol, lanolin, propylene glycol, sorbitan trioleate, polysorbate 60, triethanolamine, methylparaben, propylparaben, and perfume Flora in water; plastic squeeze bottles of 15 ml. *Mild Cream*, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a water-washable base containing stearyl alcohol, spermaceti, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of ½ and 1 ounce. *Mild Ointment*, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a petrolatum base; tubes of ½ and 1 ounce.

Consult complete product literature before prescribing.

CIBA Pharmaceutical Company
Division of CIBA-GEIGY Corporation
Summit, New Jersey 07901

2/4766 17

C I B A

LISTA DE ANUNCIANTES

1. *Burroughs Wellcome — Neosporin*
2. *Ciba — Vioform HC*
3. *Geigy Pharm. — Butazolidin*
4. *Ortho — Gravindex*
5. *Roche — Valium, Librium, Efudex, Bactrim, Dalmane*
6. *Rorer — Camalox*
7. *Schering Corp. — Valisone*
8. *Searle — Pro-Banthine*
9. *Upjohn — Unicap Therapeutic*

A N U N C I O S

LA FINANCIAL SECURITY PLANNING está solicitando médicos que estén interesados en hacer exámenes médicos de rutina para los prospectos de las compañías de seguro de vida que representan, bajo los términos siguientes: 1) Visitar y hacer dichos exámenes médicos en la oficina o residencia de cada prospecto en particular cada vez que el prospecto así lo solicite; 2) Se abonará la cantidad de \$15.00 por cada examen médico hecho completo. Para cualquier información puede comunicarse con el Sr. A. F. Irizarry García, Financial Security Planning, Oficina Núm. 303, Edificio "Grosch", Calle Comercio Núm. 402, Box 3249, Tel. 723-4755, San Juan, Puerto Rico 00904.

SE SOLICITA médico - \$24,000.00 al año — que sepa inglés, que tenga residencia y permiso para practicar la medicina en los Estados Unidos, preferible médico jubilado para supervisar BANCO DE SANGRE en Denver, Colorado. Escribir a: Blood Bank of Colorado, 1534 Blake Street, Denver, Colorado 80202. Médicos en los Estados Unidos favor de llamar al teléfono (303) 573-8586.

EL PUEBLO RURAL DE COPAHE, NEW YORK, con cerca de 2,500 residentes está en la actualidad sin un practicante general, y lo ha estado en los últimos dos años. Hay una oficina, parte de una residencia, escuelas magníficas, y actividades culturales excelentes. Se encuentran cerca Catamountshi y Tanglewood, junto con dos hospitales en Hudson, New York, y Great Barrington, Mass. Si hay alguien interesado en un ambiente tranquilo, con retiros para pacientes y amigos, esta es su oportunidad. Para información favor de escribir a: A. Schaefer, Oriole Road, Box 47, Craryville, New York 12521.

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Oficina disponible primero de septiembre o antes, 238 pies cuadrados, 730 Ponce de León. Estacionamiento disponible. Renta muy razonable. Llamar 783-8678.

Local amplio para médico dentista, 1500 pies cuadrados, primer piso, una sola escalera, en edificio 1507, Calle Loíza, final de la calle del Parque, frente a la parada de las guaguas. \$400.00 al mes de renta. Lcdo. Enrique Calderón, teléfono 722-1845, de 9 a 4 pm.

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HAAG-STREIT-900 SLIT lamp with APPLANATION.
Dr. Walter Kleis, Tel. 724-8981.

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Médico interesado en regresar a Puerto Rico cedería sus facilidades a cualquier médico que desee trabajar en Nueva York. Para más información escribir a: Dr. Sergio Peña Almodóvar, Prospect Ave., Bronx, New York.

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y no lo que deben...



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10 vitaminas combinadas con 7 minerales

Cada tableta contiene:

Vitamina A	1.5 mg.
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Mononitrato de Tiamina (B-1)	10 mg.
Riboflavina (B-2)	10 mg.
Acido Ascórbico (C) (como ascorbato de sodio)	300 mg.
Niacinamida	100 mg.
Clorhidrato de Piridoxina (B-6)	2 mg.
Pantotenato de Calcio	20 mg.
Cobalamina (B-12) (como concentrado de cobalamina)	20 mg.
Vitamina E	30 Unidades Internacionales
Hierro (a partir de 50 mg. de sulfato ferroso)	10 mg.
Yodo (como yoduro de potasio)	0.15 mg.
Calcio (como carbonato)	50 mg.
Cobre (como sulfato)	1 mg.
Manganeso (como sulfato)	1 mg.
Magnesio (como sulfato)	6 mg.
Potasio (como sulfato)	5 mg.

Posología: Adultos y niños mayores de 6 años - 1 tableta diaria.

Presentación: Frascos de 30 y 90

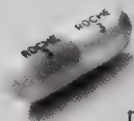
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For over 13 years, Librium has been recognized for its excellent benefits-to-risks ratio, an asset in the higher dosage ranges as in more common clinical applications. Thus, the frequency of dosage with Librium 25 mg can be flexibly adjusted to the needs and response of the individual patient, up to 100 mg daily if required. Total daily dosage for the elderly and debilitated should not exceed 20 mg. When severe anxiety has been reduced, Librium dosage should be correspondingly reduced or discontinued entirely.



basic support
in severe anxiety
Librium® 25 mg
(chlordiazepoxide HCl)
1 capsule t.i.d./q.i.d.



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Nutley, N.J. 07110

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Relief of anxiety and tension occurring alone or accompanying various diseases.

Contraindications: Patients with known hypersensitivity to the drug.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates have been reported. Use of any drug in pregnancy, lactation, or in women of childbearing age requires that its potential benefits be weighed against its possible hazards.

Precautions: In the elderly and debilitated and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruption, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function test advisable during protracted therapy.

Supplied: Librium® Capsules containing 5 mg, 10 mg or 25 mg chlordiazepoxide HCl. Libritabs® Tablets containing 5 mg, 10 mg or 25 mg chlordiazepoxide.

Boletín

Asociación médica de puerto rico

vol.65 octubre 1973 núm.10

PLAY
ELVES



ASAMBLEA ANUAL

Asociación médica de puerto rico
DEL 7 AL 10 DE NOV. 1973



HOTEL SAN JUAN

ISLA VERDE
PUERTO RICO





Everybody experiences psychic tension.



Most people can handle this tension.



Some people develop excessive psychic tension and need your counseling,



and a few may need counseling
and the psychotropic action of Valium® (diazepam).

Before deciding to make Valium (diazepam) part of your treatment plan, check on whether or not the patient is presently taking drugs and, if so, what his response has been. Along with the medical and social history, this information can help you determine initial dosage, the possibility of side effects and the ultimate prospects of success or failure.

While Valium can be a most helpful adjunct to your counseling, it should be prescribed only as long as excessive psychic tension persists and should be discontinued when you decide it has accomplished its therapeutic task. In general, when dosage guidelines are followed, Valium is well tolerated (see Dosage). For convenience it is available in 2-mg, 5-mg and 10-mg tablets.

Drowsiness, fatigue and ataxia have been the most commonly reported side effects.

Until response is determined, patients receiving Valium should be cautioned against engaging in hazardous occupations requiring complete mental alertness, such as driving or operating machinery.



Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, N.J. 07110

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

Dosage: Individualize for maximum beneficial effect.

Adults: Tension, anxiety and psychoneurotic states, 2 to 10 mg b.i.d. to q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed; adjunctively in skeletal muscle spasm, 2 to 10 mg t.i.d. or q.i.d.; adjunctively in convulsive disorders, 2 to 10 mg b.i.d. to q.i.d. **Geriatric or debilitated patients:** 2 to 2½ mg, 1 or 2 times daily initially, increasing as needed and tolerated. (See Precautions.) **Children:** 1 to 2½ mg t.i.d. or q.i.d. initially, increasing as needed and tolerated (not for use under 6 months).

Supplied: Valium® (diazepam) Tablets, 2 mg, 5 mg and 10 mg; bottles of 100 and 500. All strengths also available in Tel-E-Dose® packages of 1000.

Valium® (diazepam)

To help you manage excessive psychic tension

BOLETIN

ASOCIACION MEDICA DE PUERTO RICO



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acute arthritic inflammation...heat that freezes

In acute rheumatoid arthritis consider Tandearil. The anti-inflammatory action of Tandearil quickly helps reduce heat, pain, swelling, and stiffness. Results are usually seen in 3 or 4 days. Try it for a week when the symptoms defy aspirin control.

Remember that Tandearil is not a simple analgesic. It should not be used on patients responding to routine therapy. Before using, please read the prescribing information. It's summarized below.

Tandearil® helps take the heat off oxyphenbutazone NF Geigy

Tablets of 100 mg.

Important Note: This drug is not a simple analgesic. Do not administer casually. Carefully evaluate patients before starting treatment and keep them under close supervision. Obtain a detailed history, and complete physical and laboratory examination (complete hemogram, urinalysis, etc.) before prescribing and at frequent intervals thereafter. Carefully select patients, avoiding those responsive to routine measures, contraindicated patients or those who cannot be observed frequently. Warn patients not to exceed recommended dosage. Short-term relief of severe symptoms with the smallest possible dosage is the goal of therapy. Dosage should be taken with meals or a full glass of milk. Patients should discontinue the drug and report immediately any sign of: fever, sore throat, oral lesions (symptoms of blood dyscrasia); dyspepsia, epigastric pain, symptoms of anemia, black or tarry stools or other evidence of intestinal ulceration or hemorrhage, skin reactions, significant weight gain or edema. A one-week trial period is adequate. Discontinue in the absence of a favorable response. Restrict treatment periods to one week in patients over sixty.

Indications: Acute gouty arthritis, rheumatoid arthritis, rheumatoid spondylitis.

Contraindications: Children 14 years or less; senile patients; history or symptoms of G.I. inflammation or ulceration including severe, recurrent or persistent dyspepsia; history or presence of drug allergy; blood dyscrasias; renal, hepatic or cardiac dysfunction; hypertension; thyroid disease; systemic edema; stomatitis and salivary gland enlargement due to the drug; polymyalgia rheumatica and temporal arteritis; patients receiving other potent chemotherapeutic agents, or long-term anticoagulant therapy.

Warnings: Age, weight, dosage, duration of therapy, existence of concomitant diseases, and concurrent potent chemotherapy affect incidence of toxic reactions. Carefully instruct and observe the individual patient, especially the aging (forty years and over) who have increased susceptibility to the toxicity of the drug. Use lowest effective dosage. Weigh initially unpredictable benefits against po-

tential risk of severe, even fatal, reactions. The disease condition itself is unaltered by the drug. Use with caution in first trimester of pregnancy and in nursing mothers. Drug may appear in cord blood and breast milk. Serious, even fatal, blood dyscrasias, including aplastic anemia, may occur suddenly despite regular hemograms, and may become manifest days or weeks after cessation of drug. Any significant change in total white count, relative decrease in granulocytes, appearance of immature forms, or fall in hematocrit should signal immediate cessation of therapy and complete hematologic investigation. Unexplained bleeding involving CNS, adrenals, and G.I. tract has occurred. The drug may potentiate action of insulin, sulfonylurea, and sulfonamide-type agents. Carefully observe patients taking these agents. Nontoxic and toxic goiters and myxedema have been reported (the drug reduces iodine uptake by the thyroid). Blurred vision can be a significant toxic symptom worthy of a complete ophthalmological examination. Swelling of ankles or face in patients under sixty may be prevented by reducing dosage. If edema occurs in patients over sixty, discontinue drug.

Precautions: The following should be accomplished at regular intervals: Careful detailed history for disease being treated and detection of earliest signs of adverse reactions; complete physical examination including check of patient's weight; complete weekly (especially for the aging) or an every two week blood check; pertinent laboratory studies. Caution patients about participating in activity requiring alertness and coordination, as driving a car, etc. Cases of leukemia have been reported in patients with a history of short- and long-term therapy. The majority of these patients were over forty. Remember that arthritic-type pains can be the presenting symptom of leukemia.

Adverse Reactions: This is a potent drug; its misuse can lead to serious results. Review detailed information before beginning therapy. Ulcerative esophagitis, acute and reactivated gastric and duodenal ulcer with perforation and hemorrhage, ulceration and perforation of large bowel, occult G.I. bleeding with anemia,

gastritis, epigastric pain, hematemesis, dyspepsia, nausea, vomiting and diarrhea, abdominal distention, agranulocytosis, aplastic anemia, hemolytic anemia, anemia due to blood loss including occult G.I. bleeding, thrombocytopenia, pancytopenia, leukemia, leukopenia, bone marrow depression, sodium and chloride retention, water retention and edema, plasma dilution, respiratory alkalosis, metabolic acidosis, fatal and nonfatal hepatitis (cholestasis may or may not be prominent), petechiae, purpura without thrombocytopenia, toxic pruritus, erythema nodosum, erythema multiforme, Stevens-Johnson syndrome, Lyell's syndrome (toxic necrotizing epidermolysis), exfoliative dermatitis, serum sickness, hypersensitivity angitis (polyarteritis), anaphylactic shock, urticaria, arthralgia, fever, rashes (all allergic reactions require prompt and permanent withdrawal of the drug), proteinuria, hematuria, oliguria, anuria, renal failure with azotemia, glomerulonephritis, acute tubular necrosis, nephrotic syndrome, bilateral renal cortical necrosis, renal stones, ureteral obstruction with uric acid crystals due to uricosuric action of drug, impaired renal function, cardiac decompensation, hypertension, pericarditis, diffuse interstitial myocarditis with muscle necrosis, perivascular granulomata, aggravation of temporal arteritis in patients with polymyalgia rheumatica, optic neuritis, blurred vision, retinal hemorrhage, toxic amblyopia, retinal detachment, hearing loss, hyperglycemia, thyroid hyperplasia, toxic goiter, association of hyperthyroidism and hypothyroidism (causal relationship not established), agitation, confusional states, lethargy; CNS reactions associated with overdosage, including convulsions, euphoria, psychosis, depression, headaches, hallucinations, giddiness, vertigo, coma, hyperventilation, insomnia; ulcerative stomatitis, salivary gland enlargement. (B)98-146-800-F (10/71)

For complete details, including dosage, please see full prescribing information.

GEIGY Pharmaceuticals
Division of CIBA-GEIGY Corporation
Ardsley, New York 10502



More than sleep..

your choice of sleep medication
is wisely based on more than
sleep-inducing potential

sleep with
relative safety

Chronic tolerance studies have confirmed the relative safety of Dalmane (flurazepam HCl); no depression of cardiac or respiratory function was noted in patients administered recommended or higher doses for as long as 90 consecutive nights.

In most instances when adverse reactions were reported, they were mild, infrequent and seldom required discontinuance of therapy. Morning "hang-over" with Dalmane has been relatively infrequent. Dizziness, drowsiness, lightheadedness and the like have been the side effects noted most frequently, particularly in the elderly and debilitated. (An initial dose of Dalmane 15 mg should be prescribed for these patients.)

sleep for 7 to 8 hours
without need to
repeat dosage

No sleep medication has been as rigorously evaluated in the sleep research laboratory as Dalmane. Insomnia patients given one 30-mg capsule of Dalmane at bedtime, on average: fell asleep within 17 minutes, had fewer nighttime awakenings, spent less time awake after sleep onset, and slept for 7 to 8 hours with no need to repeat dosage during the night.

leep with
nsistency

Dalmane (flurazepam HCl) is a distinctive sleep medication—a benzodiazepine specifically indicated for insomnia. It is not a barbiturate or methaqualone, nor is it related chemically to any other sedative hypnotic.

When your evaluation of insomnia indicates the need for a sleep medication, consider Dalmane—a single entity nonnarcotic, non-habit-forming agent proved effective and relatively safe for relief of insomnia.

Dalmane has been shown to be consistently effective even during consecutive nights of administration, with no need to increase dosage.

DALMANE[®]

(flurazepam HCl)

When restful sleep is indicated

One 30-mg capsule h.s. —usual adult dosage
(15 mg may suffice in some patients)

One 15-mg capsule h.s. —initial dosage for elderly or debilitated patients.

Before prescribing Dalmane (flurazepam HCl), please consult Complete Product Information, a summary of which follows:

Indications: Effective in all types of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings and/or early morning awakening; in patients with recurring insomnia or poor sleeping habits; and in acute or chronic medical situations requiring restful sleep. Since insomnia is often transient and intermittent, prolonged administration is generally not necessary or recommended.

Contraindications: Known hypersensitivity to flurazepam HCl.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. Caution against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Use in women who are or may become pregnant only when potential benefits have been weighed against possible hazards. Not recommended for use in persons under 15 years of age. Though physical and psychological dependence have not been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage.

Precautions: In elderly and debilitated, initial dosage should be limited to 15 mg to preclude oversedation, dizziness and/or ataxia. If combined with other drugs having hypnotic or CNS-depressant effects, consider potential additive effects. Employ usual precautions in patients who are severely depressed, or with latent depression or suicidal tendencies. Periodic blood counts and liver and kidney function tests are advised during repeated therapy. Observe usual precautions in presence of impaired renal or hepatic function.

Adverse Reactions: Dizziness, drowsiness, lightheadedness, staggering, ataxia and falling have occurred, particularly in elderly or debilitated patients. Severe sedation, lethargy, disorientation and coma, probably indicative of drug intolerance or overdosage, have been reported. Also reported were headache, heartburn, upset stomach, nausea, vomiting, diarrhea, constipation, GI pain, nervousness, talkativeness, apprehension, irritability, weakness, palpitations, chest pains, body and joint pains and GU complaints. There have also been rare occurrences of sweating, flushes, difficulty in focusing, blurred vision, burning eyes, faintness, hypotension, shortness of breath, pruritus, skin rash, dry mouth, bitter taste, excessive salivation, anorexia, euphoria, depression, slurred speech, confusion, restlessness, hallucinations, and elevated SGOT, SGPT, total and direct bilirubins and alkaline phosphatase. Paradoxical reactions, e.g., excitement, stimulation and hyperactivity, have also been reported in rare instances.

Dosage: Individualize for maximum beneficial effect. *Adults:* 30 mg usual dosage; 15 mg may suffice in some patients. *Elderly or debilitated patients:* 15 mg initially until response is determined.

Supplied: Capsules containing 15 mg or 30 mg flurazepam HCl



ROCHE LABORATORIES
Div., Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

Opinion & Dialogue

"Prescription drugs – who should determine the maker?"

Dispenser of Medicine

Clifton J. Latiolais
President
American
Pharmaceutical
Association



Maker of Medicine

C. Joseph Stetler
President
Pharmaceutical
Manufacturers
Association



"Too many doctors are indifferent to the economic consequences of their decisions." So stated a recent issue of *Medical News Report* (December 4, 1972), an independent weekly newsletter published by former AMA Chief Executive F. J. L. Blasingame, M.D.

Doctor, are you indifferent...?

In discussing an anticipated increase in Blue Shield rates, Dr. Blasingame's newsletter had this to say:

"In general, it can be said, MD's have given the impression they are not particularly concerned with the increase in cost of health care to their patients...

"True, an MD's training is primarily scientific, but in the real world of practice, all of his scientific decisions have a price tag, or an economic impact. The economics of health care beckon the practitioner's attention. Concern for economics of medicine

When the pharmacist recommends that a drug product other than the one ordered be dispensed, the prescriber invariably permits the change when he feels the best interests of the patient will be served.

Shortcomings of Pro-Substitution Argument

The fact remains that it is necessary for the prescriber to know that the change is being contemplated, and to be in a position to consent or demur. Without that opportunity, the unilateral decision of the pharmacist made in the absence of clinical knowledge of the patient, could expose him to needless risks, and in addition, jeopardize the relationship between the professions of Pharmacy and Medicine. In my view, there is nothing in the pro-substitution argument that offsets these risks.

The Issue of Drug Knowledge

Substitution advocates claim that the primary justification for changing the rules is the desire to better utilize pharmacists' knowledge about drugs. Yet the pharmacist's task to keep current on the entire field of drug therapy, to some degree puts him at a disadvantage. Most often, a practicing physician will need expert knowledge of no more than 25

practice...
"Medical societies ought to con-
duct continuing campaigns to point
out the substantial savings that could
be realized thru deductible insurance
and protection for catastrophic ill-
ness. At the very least, they should, in
the patients' interest, question the
practices of any insurance organization
that raises health care costs by forc-
ing policyholders to buy insurance
they may not need or want and prob-
ably won't ever use.

"Too many doctors are indiffer-
ent to the economic consequences of
their decisions. Too many, for ex-
ample, habitually hospitalize patients
for the convenience of the MD. It's
senseless to deny such habits exist...

"Doctors, thru their medical so-
cieties, have unhesitatingly appealed
to their patients for support in the
fight against government interference
with the private practice of medicine.
And the public in the past has re-
sponded. It's time the American Med-
ical Association and state and local
medical societies paid off the debt by
decisive action to hold down the cost
of medical care."

Cost of Drugs

Insurance rates and hospital
charges are only two factors in health

care. For 30 drugs that he selects to treat the
majority of conditions encountered in
his practice. Moreover, the physi-
cian's choice of a specific brand is
based on his knowledge of the pa-
tient's medical history and current
condition, and his experiences with
the particular manufacturer's
product.

Some substitution proponents
have argued that the dispensing of a
prescription is a simple two-party
transaction between the pharmacist
and the patient, and that a substitut-
ing pharmacist may avoid even a
technical breach of contract by simply
notifying the patient that he is making
the substitution. I would judge that
few courts would be sympathetic
toward a pharmacist who substituted
without physician approval and who
undertook a legal defense that seeks
to make the patient responsible for
the pharmacist's actions.

Reduced Prescription Prices?

Substitution advocates are
suggesting to the consumer, and par-
ticularly the consumer activist, that
reduced prescription prices could
follow legalization of substitution.
We have seen absolutely no evidence
to justify this claim. To the contrary,
experience in Alberta, Canada, where
substitution is authorized, suggests

prescription and nonprescription—is
another.

And when it comes to drug
costs, the nation's pharmacists are
concerned. Through their national
professional society, the American
Pharmaceutical Association, pharma-
cists are advising the public to use
nonprescription medication cau-
tiously and conservatively, and to seek
the advice of their pharmacist before
selecting or purchasing such drugs.

Outdated Laws

The pharmacist also is aware
that when it comes to prescription
drugs, often he has an even greater
opportunity to reduce the cost to the
patient—with no sacrifice in the qual-
ity of the medication dispensed. But
in many states, outdated and anti-
quated laws prevent the pharmacist
from engaging in drug product selec-
tion. "Drug product selection" simply
means that the pharmacist functions
in the patient's interest by con-
sciously choosing, from the multiple
brands available, a low-cost quality
brand of the specific drug to be dis-
pensed in response to the physician's
prescription order.

Much *misinformation* has been
purposely spread by those who stand
to gain financially by maintaining

the opposite.

Many pharmacists understand-
ably are concerned about the cost of
maintaining multiple stocks of similar
products. While there is no doubt that
inventory costs rise when additional
brands are stocked, it would be inter-
esting to know how much they rise,
and how many pharmacists actually
stock *all* brands—of, say, ampicillin
or tetracycline—or how long they
keep "slow moving" products on their
shelves before they are returned for
credit. To ask that the industry elimi-
nate multiple sources is to ask com-
petitors to stop competing.

Drug Substitution—A License for the Unethical

Anti-substitution repeal would
favor "corner cutting" pharmacists
and manufacturers. For them, free
substitution would be not a right, but
a license. As an aftermath, it is quite
likely that the confidence of both phy-
sicians and patients in the profession
of Pharmacy would be eroded, as
revelations about the unconscionable
behavior of an undisciplined few were
magnified in the press or in profes-
sional circles.

Summary

In short, what the American
Pharmaceutical Association advo-

less stream of propaganda has ema-
nated from the drug industry in an
effort to persuade the medical profes-
sion that these so-called anti-substitu-
tion laws should be retained. And as
long as these laws are retained, the
drug industry will continue its current
marketing practices which contribute
unnecessarily to high drug costs to
patients. These practices also are in-
viting government agencies to expand
their restrictive controls on physi-
cians and pharmacists.

APhA Efforts

As pharmacists, we are con-
cerned about health care costs. We
hope that every physician shares our
concern on this vital issue, and will
give his personal support to the con-
structive efforts APhA has undertaken
in the interest of all patients.

*(For a complete discussion of
drug product selection, you are invited
to request a free copy of the "White
Paper on the Pharmacist's Role in
Product Selection" from: American
Pharmaceutical Association,
2215 Constitution Avenue, N.W.,
Washington, D.C. 20037.)*

cates as a broad-spectrum panacea
looks to us to be not only a minority
view (advocacy of substitution is by
no means a uniform policy in Phar-
macy), but also an extraordinarily
costly and ineffective remedy, whose
side effects are odious. We believe
(1) that an impressive majority of
pharmacists prefer to work with
Medicine and with industry, for the
consumer, and for the general good,
(2) that they seek the privilege to sub-
stitute when the patient might gain
and when the patient's doctor agrees,
and (3) that they seek to work for the
resolution of genuine grievances
openly and professionally.

*(For amplification of PMA views,
please write for our booklet, "The
Medications Physicians Prescribe:
Who Shall Determine the Source?"
It is available from: Pharmaceutical
Manufacturers Association, 1155
Fifteenth Street, N.W., Washington,
D.C. 20005.)*

Pharmaceutical
Manufacturers Association
1155 Fifteenth Street, N.W.
Washington, D.C. 20005



ROCHE announces new

BACTRIMTM

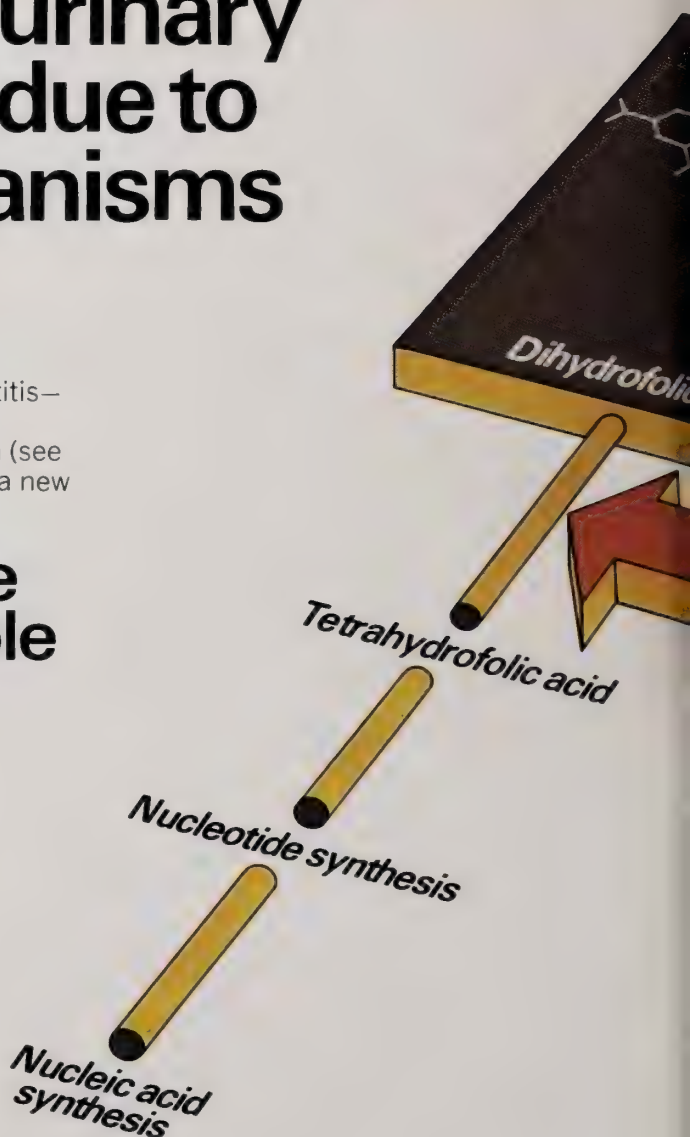
Each tablet contains 80 mg trimethoprim and 400 mg sulfamethoxazole.

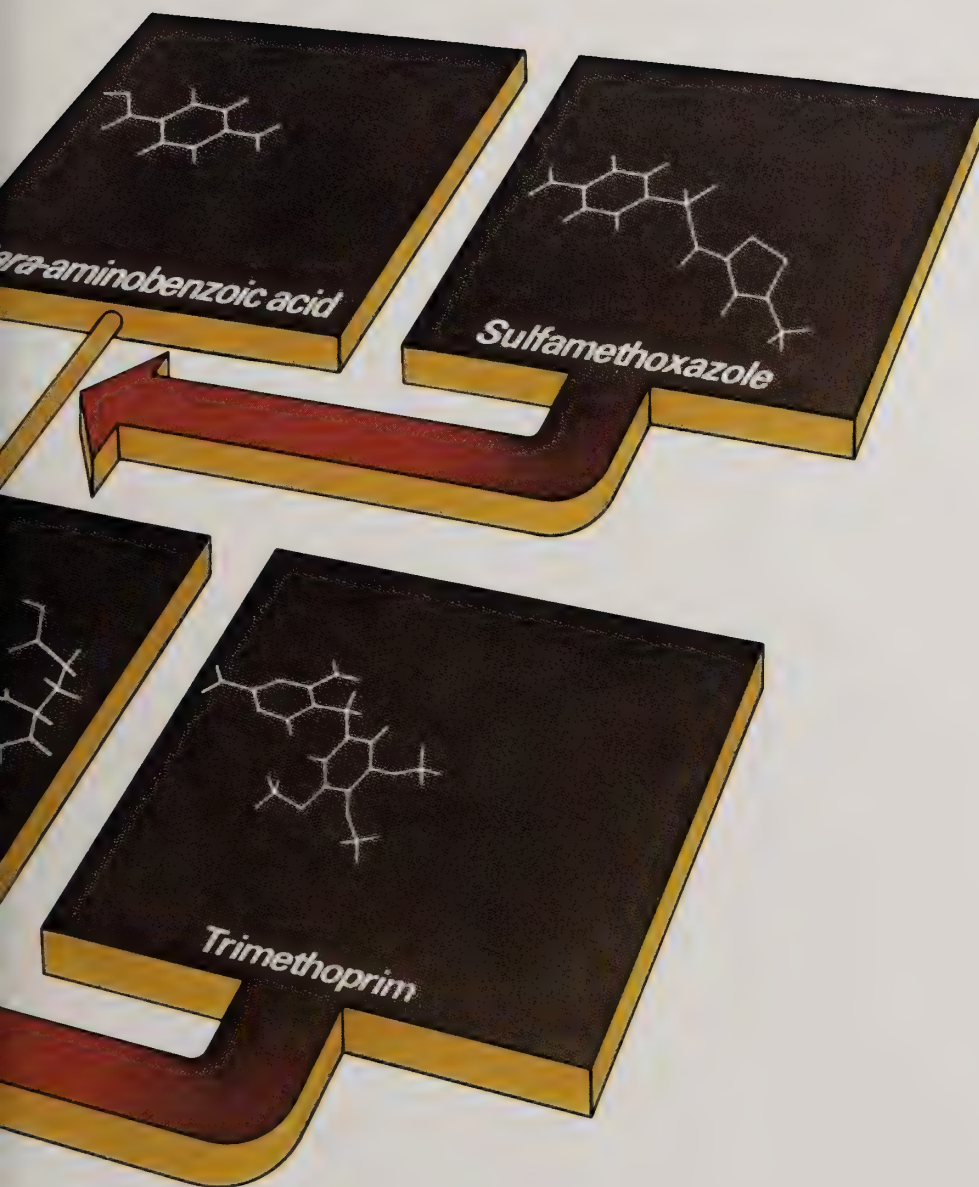
a new type of antibacterial for a two-pronged attack against chronic urinary tract infections due to susceptible organisms

Bactrim is highly effective in the treatment of these infections – primarily pyelonephritis, pyelitis and cystitis – when due to susceptible organisms. This efficacy is related to the unique mode of action against bacteria (see illustration), an action that, in effect, makes Bactrim a new type of antibacterial.

Bactrim interrupts the life cycle of susceptible bacteria

Unique mode of action interrupts the life cycle at two important points, thereby impeding the production of nucleic acids and proteins essential to these bacteria. These consecutive interruptions occur because sulfamethoxazole and trimethoprim resemble naturally existing substrates. By competitive replacement of these substrates, they inhibit further synthesis.





new **BACTRIM**TM

Each tablet contains 80 mg trimethoprim and 400 mg sulfamethoxazole.

for chronic urinary tract infections

Before prescribing, please see complete product information on last page of advertisement.

Excellent clinical response in chronic urinary tract infections even with obstructive complications

A multiclinic, double-blind study* of response to a ten-day course of therapy in 471[†] patients with chronic urinary tract infections demonstrated the superiority of Bactrim. On the 10th day after initiation of therapy, 91.7% (of 168 patients) showed significant bacteriological response to Bactrim, compared with 81.2% (of 144 patients) to trimethoprim and 64.5% (of 155 patients) to sulfamethoxazole. More than half of these patients had obstructive complications.

Excellent response maintained

Bactrim proved equally impressive in maintaining this bacteriological response. In the above study, after a ten-day course of therapy with Bactrim, 68.4% of patients with chronic urinary tract infections *maintained* response for up to 42 consecutive days, compared with 59.7% with trimethoprim and 44.4% with sulfamethoxazole. These results are particularly noteworthy considering the number of patients with obstructive complications—cases regarded as being notoriously difficult to treat.

Prescribing considerations

Clinical Limitations: Currently, the increasing frequency of resistant organisms is a limitation of the usefulness of all antibacterial agents, especially in the treatment of chronic and recurrent urinary tract infections. Not recommended for children under twelve.

Contraindications: Hypersensitivity to trimethoprim or sulfonamides. Pregnancy and during the nursing period.

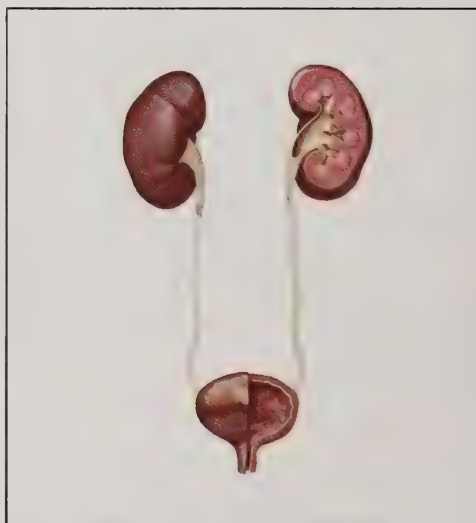
Warnings and Precautions: Both sulfamethoxazole and trimethoprim have been reported to interfere with hematopoiesis. Complete blood counts should be done frequently. If a significant reduction in the count of any formed blood element is noted, Bactrim should be discontinued. Bactrim should be given with caution to patients with impaired renal or hepatic function, possible folate deficiency, severe allergy or bronchial asthma. Maintain adequate fluid intake. Urinalyses with careful microscopic examination and renal function tests should be performed during therapy, particularly for those patients with impaired renal function.

Adverse Effects: Among the most common side effects are nausea, vomiting, rash, leukopenia and elevations in SGOT and creatinine.

Usual adult dosage: two tablets every twelve hours for 10 to 14 days; no loading dose required.

*Data on file, Hoffmann-La Roche Inc., Nutley, N.J. 07110

[†]4 patients not available for evaluation at day 10.



new

BACTRIMTM

Each tablet contains 80 mg trimethoprim and 400 mg sulfamethoxazole.

for chronic urinary tract infections



Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, N.J. 07110

Complete Product Information:

Description: Bactrim is a synthetic antibacterial combination product, available in scored light-green tablets, each containing 80 mg trimethoprim and 400 mg sulfamethoxazole.

Trimethoprim is 2,4-diamino-5-(3,4,5-trimethoxybenzyl) pyrimidine. It is a white to light-yellow, odorless, bitter compound with a molecular weight of 290.3.

Sulfamethoxazole is N¹-(5-methyl-3-isoxazolyl)sulfanilamide. It is almost white in color, odorless, tasteless compound with a molecular weight of 253.28.

Actions: Microbiology: Sulfamethoxazole inhibits bacterial synthesis of dihydrofolic acid by competing with *para*-aminobenzoic acid. Trimethoprim blocks the production of tetrahydrofolic acid from dihydrofolic acid by binding to and reversibly inhibiting the required enzyme, dihydrofolate reductase. Thus, Bactrim blocks two consecutive steps in the biosynthesis of nucleic acids and proteins essential to many bacteria.

In vitro studies have shown that bacterial resistance develops more slowly with Bactrim than with trimethoprim or sulfamethoxazole alone.

In vitro serial dilution tests have shown that the spectrum of antibacterial activity of Bactrim includes the common urinary tract pathogens with the exception of *Pseudomonas aeruginosa*. The following organisms are usually susceptible: *Escherichia coli*, *Klebsiella-Enterobacter*, *Proteus mirabilis* and indole-positive proteus species.

Representative Minimum Inhibitory Concentration Values for Bactrim-Susceptible Organisms (MIC—mcg/ml)				
Bacteria	Trimethoprim alone	Sulfamethoxazole alone	TMP/SMX (1:20) TMP SMX	
<i>Escherichia coli</i>	0.05—1.5	1.0 —245	0.05—0.5	0.95— 9.5
<i>Proteus</i> spp. indole positive	0.5 —5.0	7.35 —300	0.05—1.5	0.95—28.5
<i>Proteus mirabilis</i>	0.5 —1.5	7.35 — 30	0.05—0.15	0.95— 2.85
<i>Klebsiella-Enterobacter</i>	0.15—5.0	0.735—245	0.05—1.5	0.95—28.5

Human Pharmacology: Bactrim is rapidly absorbed following oral administration. The blood levels of trimethoprim and sulfamethoxazole are similar to those achieved when each component is given alone. Peak blood levels for the individual components occur one to four hours after oral administration. The half-lives of sulfamethoxazole and trimethoprim, 10 and 16 hours respectively, are relatively the same regardless of whether these compounds are administered as individual components or as Bactrim. Detectable amounts of trimethoprim and sulfamethoxazole are present in the blood 24 hours after drug administration. Free sulfamethoxazole and trimethoprim blood levels are proportionately dose-dependent. On repeated administration, the steady-state ratio of trimethoprim to sulfamethoxazole levels in the blood is about 1:20.

Sulfamethoxazole exists in the blood as free, conjugated and protein-bound forms; trimethoprim is present as free, protein-bound and metabolized forms. The free forms are considered to be the therapeutically active forms. Approximately 44 percent of trimethoprim and 70 percent of sulfamethoxazole are protein-bound in the blood. The presence of 10 mg percent sulfamethoxazole in plasma decreases the protein binding of trimethoprim to an insignificant degree; trimethoprim does not influence the protein binding of sulfamethoxazole.

Excretion of Bactrim is chiefly by the kidneys through both glomerular filtration and tubular secretion. Urine concentrations of both sulfamethoxazole and trimethoprim are considerably higher than are the concentrations in the blood. When administered together as in Bactrim, neither sulfamethoxazole nor trimethoprim affects the urinary excretion pattern of the other.

Indications: Chronic urinary tract infections (primarily pyelonephritis, pyelitis and cystitis) due to susceptible organisms (usually *E. coli*, *Klebsiella-Enterobacter*, *Proteus mirabilis*, and, less frequently, indole-positive proteus species).

Important note: Currently, the increasing frequency of resistant organisms is a limitation of the usefulness of all antibacterial agents, especially in the treatment of chronic and recurrent urinary tract infections.

Contraindications: Hypersensitivity to trimethoprim or sulfonamides. Pregnancy and during the nursing period (see Reproduction Studies).

Warnings: Deaths associated with the administration of sulfonamides have been reported from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias. Experience with trimethoprim alone is much more limited, but it has been reported to interfere with hematopoiesis in occasional patients. In elderly patients concurrently receiving certain diuretics, primarily thiazides, an increased incidence of thrombopenia with purpura has been reported.

The presence of clinical signs such as sore throat, fever, pallor, purpura or jaundice may be early indications of serious blood disorders. Complete blood counts should be done frequently in patients receiving Bactrim. If a significant reduction in the count of any formed blood element is noted, Bactrim should be discontinued.

At the present time, there is insufficient clinical information on the use of Bactrim in infants and children under 12 years of age to recommend its use.

Precautions: Bactrim should be given with caution to patients with impaired renal or hepatic function, to those with possible folate deficiency and to those with severe allergy or bronchial asthma. In glucose-6-phosphate dehydrogenase-deficient individuals, hemolysis may occur. This reaction is frequently dose-related. Adequate fluid intake must be maintained in order to prevent crystalluria and stone formation. Urinalyses with careful microscopic examination and renal function tests should be performed during therapy, particularly for those patients with impaired renal function.

Adverse Reactions: For completeness, all major reactions to sulfonamides and to trimethoprim are included below, even though they may not have been reported with Bactrim.

Blood dyscrasias: Agranulocytosis, aplastic anemia, megaloblastic anemia, thrombopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia.

Allergic reactions: Erythema multiforme, Stevens-Johnson syndrome, generalized skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis.

Gastrointestinal reactions: Glossitis, stomatitis, nausea, emesis, abdominal pains, hepatitis, diarrhea and pancreatitis.

C.N.S. reactions: Headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo, insomnia, apathy, fatigue, muscle weakness and nervousness.

Miscellaneous reactions: Drug fever, chills, and toxic nephrosis with oliguria and anuria. Periarteritis nodosa and L. E. phenomenon have occurred.

The sulfonamides bear certain chemical similarities to some goitrogens, diuretics (acetazolamide and the thiazides) and oral hypoglycemic agents. Goiter production, diuresis and hypoglycemia have occurred rarely in patients receiving sulfonamides. Cross-sensitivity may exist with these agents. Rats appear to be especially susceptible to the goitrogenic effects of sulfonamides, and long-term administration has produced thyroid malignancies in the species.

Dosage and Administration: Not recommended for use in children under 12 years of age.

The usual adult dosage is two tablets every 12 hours for 10 to 14 days.

For patients with renal impairment:

Creatinine Clearance (ml/min)	Recommended Dosage Regimen
Above 30	Usual standard regimen
15-30	2 tablets every 24 hours
Below 15	Use not recommended

How Supplied: Tablets, containing 80 mg trimethoprim and 400 mg sulfamethoxazole—bottles of 100 and 500; Tel-E-Dose® packages of 1000; Prescription Paks of 40, available singly and in trays of 10. Imprint on tablets: ROCHE 50.

Reproduction Studies: In rats, doses of 533 mg/kg sulfamethoxazole or 200 mg/kg trimethoprim produced teratological effects manifested mainly as cleft palates. The highest dose which did not cause cleft palates in rats was 512 mg/kg sulfamethoxazole or 192 mg/kg trimethoprim when administered separately. In two studies in rats, no teratology was observed when 512 mg/kg of sulfamethoxazole was used in combination with 128 mg/kg of trimethoprim. However, in one study, cleft palates were observed in one litter out of 9 when 355 mg/kg of sulfamethoxazole was used in combination with 88 mg/kg of trimethoprim.

In rabbits, trimethoprim administered by intubation from days 8 to 16 of pregnancy at dosages up to 500 mg/kg resulted in higher incidences of dead and resorbed fetuses, particularly at 500 mg/kg. However, there were no significant drug-related teratological effects.

BACTRIM

Each tablet contains 80 mg trimethoprim and 400 mg sulfamethoxazole.



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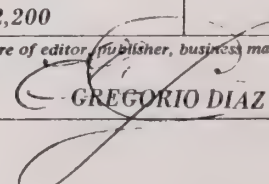
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PROGRAMA ASAMBLEA ANUAL

JEVES 8 DE NOV. DE 1973 **SALON ISLA VERDE**
SECCION "B" - 9:00 am

SECCION DE GASTROENTEROLOGIA

Juan T. Tomasini, MD, Moderador

00 "Ultraestructura de la Gastritis Atrófica Inducida"

A. Rodríguez Olleros, MD

A. Martínez Palomo, MD

J. F. Taveras, MD

F. Febles Vizcarrondo, MD

20 Parabiotic Perfusion and Dialysis in Experimental
Hepatic Coma

E. A. Santiago Delpín, MD

C. O. Callender, MD

A. Moberg, MD

C. M. Kjellstrand, MD

J. S. Najarian, MD

40 Ectopic Drainage of Common Bile Duct

E. Vázquez Quintana, MD

0:00 Enfermedad Hepática en Donantes Positivos para el
Antígeno de la Hepatitis B

Carlos E. Rubio, MD

Ibrahim Pérez, MD

Ricardo Martínez, MD

Ruth M. Quiñones, BS

0:20 Estudios Dinámicos del Esófago con Radioisótopos
de Vida Media Corta

Aldo E. Lanaro, MD

Antonio Bosch, MD

René C. Dietrich, MD

0:40 Receso

0:50 Schistosoma Mansonii — Radiological Manifestations

Heriberto Pagán Sáez, MD

1:10 Enteropathogenic Intestinal Bacteria in Tropical Sprue

J. J. Corcino, MD

F. A. Klipstein, MD

L. V. Holdeman, MD

W. E. C. Moore, MD

11:30 Conferencia Magistral Dr. Ramón J. Sifre
"Inflammatory Disease of the Bowel"

Howard M. Spiro, MD

Presentación a cargo de: *Federico Hernández
Morales, MD*

Auspician: Sociedad Puertorriqueña de Gastro-
enterología y Sección de Gastroenterología de
la AMPR - Warren Teed Pharmaceuticals

12:30 Accupunture Recent Concepts

John J. Bonica, MD

1:15 pm Almuerzo - Salón Tropicoro

SEMINAR ON IMMUNOLOGY

Michael Frank, MD

*This seminar is sponsored by the Section on Allergy and Im-
munology of the Puerto Rico Medical Association*

2:30 pm 1) Structure and Biological Activity of Immuno-
globulins

3:30 2) Complement

4:00 3) Delayed Hypersensitivity and Cell Mediated
Reactions

JUEVES 8 DE NOV. de 1973

SALON ISLA VERDE

SECCION "C-D"

9:00 am

CAPITULO DE PUERTO RICO DE LA INDUSTRIAL MEDIC ASSOCIATION

Luis J. Flores Vilar, MD, Moderador

9:00 Introducción y Presentación de los Conferenciantes
Hiram Vázquez Milán, MD

9:15 Valor de la Electromiografía en los Lesionados de
la Industria
Domingo Cerra, MD

9:30 Contribución de la Electroencefalografía en los
Lesionados de la Industria
Luis Pío Sánchez Longo, MD

- 9:45 Quemaduras Eléctricas de la Mano
José F. Bernal, MD
- 10:00 La Ortopedia en el Tratamiento del Lesionado de la Industria
Aníbal Lugo, MD
- 10:15 Receso
- 10:30 Rehabilitación del Paciente Cardíaco
Herman Flax, MD
- 10:45 Lesiones de la Mano en la Industria
Efraín Torres Castaing, MD
- 11:00 El Hospital, el Ejecutivo y la Medicina Industrial
Eduardo Montilla, MD
- 11:15 La Neurología en la Medicina Industrial
Juan Rodríguez del Valle, MD
- 11:30 La Neurocirugía en los Accidentes de Trabajo
Guillermo Nuñez Oti, MD
- 11:45 La Nueva Ley Norteamericana Sobre Enfermedades Ocupacionales
Rafael Peñalver, MD
- 12:30 Almuerzo — Salón Tropicoro

JUEVES 8 DE NOV. DE 1973

SALON BARON'S
9:00 am

SECCION DE MEDICINA INTERNA

Norman Maldonado, MD, Moderador

- 9:00 Osteítis Fibrosa Cística Generalisada
Gabriel R. Martínez Rovira, MD
Aureo García Bulls, MD
- 9:20 El Síndrome de la Silla Turca Vacía - Un Estudio Clínico, Endocrino y Radiológico.
Agustín M. de Andino, MD
Luis R. Guzmán López, MD
Gabriel Martínez Rovira, MD
Emilio Torres Reyes, MD

- 9:40 Successful Heparin Therapy of Meningococcemic Coagulopathy and Microangiopathy
Antonio J. Grillo López, MD
Enrique Vélez García, MD
Jean Fradera, MD
Norman Maldonado, MD
- 10:00 NBT: Resultados con Inmunosupresión Experimental
Alberto J. Larrieu, MD
Magda S. Rodríguez, MT, ASCP
Eduardo A. Santiago Delpín, MD, MS
- 10:20 Bactericidal Activity of Ascitic Fluid
Ramón H. Bermúdez, MD
E. Waddell, BS
M. A. Medina, MS
G. A. Ramírez de Arellano, MD
- 10:40 Receso
- 11:00 Síndrome de Isquemia del Tronco Cerebral por Traumatismo de la Arteria Vertebral
Oscar Tejeda, MD
- 11:20 Problem Oriented Record — Discusión a Panel: El Record por Problema
Introducción — *E. A. Ramírez, MD, MS*
Data Base — *F. Burgos, MD*
Problema Formulación y Planes: *J. V. Rivera, MD*
Notas y Ordenes — *R. Bermúdez, MD*
Resumen Clínico — *F. Córdova, MD*
Aplicación a la Práctica Ambulatoria:— *M. Cáceres de Costas, MD*
Preguntas y Discusión
- 12:30 Almuerzo — Salón Tropicoro

VIERNES 9 DE NOV. DE 1973

SALON ISLA VERDE
SECCION "B" - 9:00 am*Manuel Martínez Maldonado, MD, Moderador*

- 9:00 Evaluation of Renal Function
Jack Metcalf, MD

90	Renal Dynamic Study (99 M TC-DTPA) in the Evaluation of Renal Diseases <i>Julio V. Rivera, MD</i> <i>A. L. Rodríguez Rosado, MD</i> <i>Justo González, MD</i>	12:45	Almuerzo — Salón Tropicoro
		VIERNES 9 DE NOV. DE 1973	SALON ISLA VERDE SECCION "C-D" 9:00 am
0	Incidental Renal Scans in Patients Undergoing Brain Scans with Per technetate DTPA <i>A. L. Rodríguez Rosado, MD</i> <i>Julio V. Rivera, MD</i>		<i>Herman Flax, MD, Moderador</i>
10	Importance of the Application of Electron and Immunofluorescent Microscopy to the Study of Kidney Diseases <i>Jesús M. Vázquez Urrutia, MD</i> <i>Gustavo Ramírez de Arellano, MD</i> <i>Oswaldo Ramírez Muxó, MD</i> <i>José L. Cangiano, MD</i> <i>Rafael Ramírez González, MD</i> <i>José Campos, MD</i>	9:00	Panel: Dolor de Espalda desde el Punto de Vista Fisiátrico Moderador: <i>Rafael Berrios Martínez, MD</i> Anatomía de la Columna Vertebral <i>Felipe J. Lleras Santos, DDS</i> Causas Más Comunes del Dolor de Espalda <i>Rafael Berrios Martínez, MD</i> Electromiografías en Pacientes con Dolor de Espalda <i>Florencio Sáez, MD</i> Tratamientos de Dolor de Espalda <i>Herman Flax, MD</i> Preguntas y Respuestas
30	Acute Glomerulonephritis — Newer Concepts <i>Jack Metcalf, MD</i>		
50	Receso		
10	Síndrome Nefrótico <i>Gerardo del Río Pérez, MD</i>	10:00	Receso
30	Uremic Non Malignant Hypertension: Mechanisms and Treatment <i>José L. Cangiano, MD</i> <i>Oswaldo Ramírez Muxó, MD</i> <i>Rafael Ramírez González, MD</i> <i>Arturo Trevino, BS</i> <i>José A. Campos, MD</i>	10:20	The New Doctrine as to Physician Responsibility in Puerto Rico: The Meaning of the Oliveros Decision <i>John L. Simon, MD</i>
		10:40	Treatment of Soft Tissue Injuries in Maxillofacial Trauma <i>Miguel R. Alonso, MD</i>
0	Renal Dysfunction Associated with Methoxyflurane Anesthesia <i>Carlos A. Vaamonde, MD</i> <i>A. R. Satyanathan, MD</i> <i>J. L. Hotchkiss, MD</i> <i>V. Fiserova-Bergerova, PhD</i> <i>D. A. Holaday, MD</i>	11:00	Microcirugía de la Laringe <i>José Picó, MD</i> <i>Nelson Fernández Blasini, MD</i>
20	Nefrotoxicidad de la Combinación de Cephalothin-Gentamicina <i>Fernando Cabanillas, MD</i> <i>Rafael Burgos, MD</i> <i>Roberto Rodríguez, MD</i> <i>César Baldizón, MD</i>	11:20	Panel: La Contaminación Ambiental y los Efectos Nocivos en la Salud Auspicio: Asociación Puertorriqueña Antituberculosa y Salud Respiratoria <i>Jaime F. Pou, MD, Moderador</i> Participantes: <i>Herminio Lugo Lugo, PhD</i> <i>Edmundo Figueras, MD</i> <i>Pedro Mayol, MD</i>
		12:45	Almuerzo — Salón Tropicoro

VIERNES 9 DE NOV. DE 1973

SALON BARON'S
9:00 am*Francisco Muñiz, MD, Moderador*

- 9:00 Cell Mediated Reactions, Immunological Deficiency Diseases and Defects in Delayed Hypersensitivity
Michael Frank, MD
- 9:30 Immunologic Studies with Schistosomiasis Mansoni
Nilda Hernández-Almenas, BS
George V. Hillyer, PhD
- 9:50 Humoral Reactions, Diseases Associated with Abnormal Antibodies, Complement Mediated Illnesses and Problems of Immediate Hypersensitivity
Michael Frank, MD
- 10:20 Prospects for the Immunotherapy of Cancer
Richard L. Simmons, MD
- 10:50 Receso
- 11:00 Estimulación Antigénica de Linfocitos por Células Malignas de Linfoma: Evidencia de un Nuevo Antígeno Tumoral
Fernando Cabanillas, MD
Marisel Roque, BSMT
Francisco Muñiz, MD
- 11:20 La Gamagrafía con 67 GA en el Estudio de Pacientes con Linfomas
Aldo E. Lanaro, MD
René Dietrich, MD
Enrique Vélez García, MD
- 11:40 Chemotherapy of Gastrointestinal Cancer Experience in 100 Patients
Julio A. Morales Rivera, MS IV
Antonio J. Grillo López, MD
Enrique Vélez García, MD
- 12:00 Combination Chemotherapy for Disseminated Carcinoma of the Breast
José A. Lozada, MD
Antonio J. Grillo López, MD
Enrique Vélez García, MD
- 12:20 Evaluation of Continuous 5-Fluorouracil in Cancer Therapy

A. J. Grillo López, MD
E. Vélez García, MD

12:45 Almuerzo — Salón Tropicoro

SABADO 10 DE NOV. DE 1973

SALON ISLA VERDE
SECCION "B"
9:00 am*Luis A. Román Irizarry, MD, Moderador*

- 9:00 Determinación de la Perfusión Pulmonar en la Tetralogía de Fallot Mediante la Gamagrafía
René C. Dietrich, MD
Jorge Sánchez, MD
Aldo Lanaro, MD
A. Martínez Picó, MD
- 9:20 Accelerated Idioventricular Rhythm During Pregnancy: A Report of Two Cases
Juan M. Aranda, MD
Francisco Veray, MD
- 9:40 Stress Testing: Current Concepts and Experience at the San Juan Veterans Hospital
Esteban Linares Rivera, MD
E. A. Ramírez, MD
J. Pereyó, MD
- 10:00 The Effect of Spread of Excitation on the Cardiovascular System During Prolonged Isometric Exercise
Marcos U. Ramos, MD
- 10:40 Receso
- 11:00 The Role of Selective Coronary Arteriography in the Management of Chest Pain
José A. Pereyó, MD
Esteban Linares Rivera, MD
Elí A. Ramírez, MD
- 11:20 Comparison of Minnesota Impedance Cardiograph and Electrocardiograph in Bicycle Stress Testing in Early Post Myocardial Infarction Patients
Marcos Ramos, MD
John LaBree, MD
W. Remole, MD
W. G. Kubicek, MD
F. J. Kottke, MD

11:40 Treatment of Congestive Heart Failure
Albert N. Brest, MD

12:20 Transthoracic Electrical Impedance as a Clinical
Guide of Pulmonary Fluid Accumulation in
Congestive Heart Failure
Marcos U. Ramos, MD
John W. LaBree, MD
William G. Kubicek, PhD

12:40 Conferencia Magistral "Ramón M. Suárez"
"Relaciones Entre Automatismo y Conducción
en los Bloqueos Cardíacos"
Mauricio Rosenbaum, MD

1:30 Almuerzo y Toma de Posesión del Quincuagésimo
Segundo Presidente de la AMPR - *Rosa E. Fiol, MD*,
Salón Isla Verde

RESUMENES DE TRABAJOS PRESENTADOS EN EL PROGRAMA CIENTIFICO

BACTERICIDAL ACTIVITY OF ASCITIC FLUID

Bermúdez, R. H., MD, Waddell, E., MD, Medina, M. A., MD, and Ramírez de Arellano, G. A., MD., Veterans Administration Hospital and the University of P. R. School of Medicine, San Juan, Puerto Rico.

The bactericidal activity of fresh ascitic fluid obtained from patients with various illnesses was compared with their own serum and sera from healthy individuals. Both serum-resistant and serum-sensitive strains of *Escherichia coli* were studied as well as other gram-positive and gram-negative organisms. The test system consisted of incubating approximately 100,000 organisms with ascitic fluid at 37°C and performing bacterial counts at hourly intervals by the plate dilution method. Serum-sensitive bacteria were killed in approximately four hours and no serum-sensitive bacteria survived in ascitic fluid. Serum-resistant strains of *E. coli* survived in ascitic fluid for periods of over eight hours, but were no longer viable at twenty-four hours. *Staphylococci* multiplied and survived in both sera and ascitic fluid. The bactericidal activity of fresh ascitic fluid parallels that of human sera. The cells contained in ascitic fluid did not significantly influence bactericidal activity. Complement appeared to play a role in bacterial killing. The treatment of bacterial peritonitis in the presence of ascites should include an antistaphylococcal antibiotic agent.

NBT: RESULTADOS CON INMUNOSUPRESION EXPERIMENTAL

Alberto J. Larrieu, MD, Magda S. Rodríguez, MT, ASCP, Eduardo A. Santiago Delpín, MD, MS. Depto. Cirugía, Esc. Med. UPR.

Células polimorfonucleares (PMN) aumentan su habilidad para reducir el Nitroblue tetrazolium (NBT) durante infecciones bacterianas. Es útil para diagnosticar infecciones bacterianas y para seguimiento de

pacientes inmunosuprimidos. Sin embargo, la literatura presenta estudios conflictivos en el uso de NBT en estos pacientes. Hemos estudiado la respuesta de perros con infección a NBT.

Hicimos NBT en perros saludables, antes, y cinco horas después de la inyección intravenosa de 1cc/kg de un cultivo de *E. coli* de 18 horas. Grupo I (control) demostró 4.4 por ciento antes, y 10 por ciento, 5 horas después en NBT (p.02). Grupo II recibió metilprednisolona (30 mg/kg 1 hora antes de la infección, y demostró 4 por ciento antes y 3 por ciento, 5 horas después de la infección (N. S.) Grupo III recibió prednisona 2mg/kg diario por 5 días antes del experimento, y demostró 2.5 por ciento antes y 12.3 por ciento, 5 horas después de la infección (p .001). Grupo IV recibió azotiaprima 3 mg/kg diario por 5 días antes de la infección, y demostró 3.2 por ciento antes y 11.2 por ciento, 5 horas después de la infección (p .001). Grupo V recibió prednisona 2 mg/kg diario por 30 días antes del experimento, y demostró 5 por ciento antes y 4.7 por ciento, 5 horas después de la infección (N.S.). Grupo VI recibió azotiaprima 3 mg/kg diario por 30 días antes de la infección, y mostró 3.5 antes, y 3.9 por ciento después de la infección (N.S.).

Metilprednisolona en dosis altas, y prednisona y azotiaprima crónicamente, alteran la habilidad del PMN para reducir NBT. Cursos cortos (5 días) de prednisona y azotiaprima aparentemente no alteran la respuesta de NBT.

SUCCESSFUL HEPARIN THERAPY OF MENINGOCOCCIC COAGULOPATHY AND MICROANGIOPATHY

Antonio J. Grillo-López, MD, Enrique Vélez-García, MD, Jean Fradera, BS, MT, and Norman Maldonado, MD., Hematology Section, Department of Medicine, University of Puerto Rico School of Medicine.

No infectious agent can kill a human being quicker than the meningococcus. Undoubtedly, the term

"fulminant meningococcemia" is well justified. In recent years it has become increasingly apparent that the intractability and irreversibility of fatal cases of meningococcemia are intimately related to the occurrence of disseminated intravascular coagulation (DIC). Microangiopathic hemolytic anemia (MAHA), a hemolytic process characterized by anemia, thrombocytopenia, and the presence of traumatic erythrocytes in peripheral blood, has been described to occur concurrently with DIC in a large proportion of cases. Anticoagulation with heparin has been proposed as the treatment of choice for both DIC and MAHA. We have studied two cases of meningococcemia which are reported here; both had DIC, one had MAHA, and were successfully treated with heparin. The pathogenesis of DIC and MAHA is presented. The rationale for heparin therapy as well as the pro's and con's of this controversial subject are discussed

EL SINDROME DE LA SILLA TURCA VACIA: UN ESTUDIO CLINICO, ENDOCRINO Y RADIOLOGICO

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El agrandamiento radiológico de la silla turca ha sido considerado por los especialistas en la materia como el resultado final del crecimiento de un tumor pituitárico intrasillar. Ocasionalmente, este hallazgo ha sido interpretado como consecuencia de un tumor suprasillar, de un meningioma del túbulo de la silla o de un aneurisma intrasillar de la arteria carotídea.

Recientemente el nombre de "silla turca vacía" ha sido usado por anatomistas y neuroradiólogos para describir la presencia de una silla granadada asociada con una glándula pituitaria pequeña o atrófica. La confirmación definitiva de este diagnóstico descansa en los resultados obtenidos en la exploración pneumoencefalográfica o en aquellos obtenidos en la exploración neuroquirúrgica.

Durante los últimos tres años los autores han tenido la oportunidad de observar cuidadosamente cinco pacientes, todas mujeres, representando diferentes estadios de este interesante síndrome, desde aquella con ningún síntoma clínico hasta aquella que llega al neurocirujano con una rinorrea de líquido cefalorraquídeo. El cuadro clínico, endocrino y radiológico ha sido estudiado en estos casos, tratando de determinar en cada uno el posi-

ble factor etiológico. En general el cuadro clínico se caracteriza por una escasez de síntomas y signos, con la excepción de cefaleas irregulares de intensidad variable, amenorreas intermitentes, ligero hipotiroidismo o rinorrea de líquido cefalorraquídeo. El estudio endocrino reveló existencia de disfunción pituitaria mínima en tres de los cinco casos. No se observó casos de compromiso visual debido a presión quiasmática en ningún caso. Los autores presentarán sus recomendaciones en cuanto al seguimiento de estos casos debido a las complicaciones que pueden ocurrir en el curso de la enfermedad.

OSTEITIS FIBROSA CISTICA GENERALISATA

Gabriel R. Martínez Rovira, MD y Aureo García Bulls, MD, Doctors Medical Center y Hospital San Jorge.

Aunque el hiperparatiroidismo primario manifestado por la clásica osteitis fibrosa quística era rara vez diagnosticada en el pasado, nuevos conceptos químicos y detección bioquímica de rutina en pacientes asintomáticos han hecho posible reconocer con más frecuencia esta interesante condición.

Recientemente estudiamos un paciente de mediana edad que presentó, con pérdida de peso, dolor abdominal e hipercalcemia. Estudios radiológicos demostraron una lesión polipoide gástrica, múltiples radiolucencias quísticas en varios huesos y una masa en la periferia del campo pulmonar derecho. Estudios clínicos y químicos, biopsia ósea y pulmonar y exploración del cuello confirmaron el diagnóstico de enfermedad de von Recklinhausen y tumor pardo pulmonar ("brown tumor") causado por un adenoma gigante de paratiroide.

NEFROTOXICIDAD DE LA COMBINACION DE CEPHALOTHIN-GENTAMICINA

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Mientras recibían terapia con una combinación de Cephalothin y Gentamicina, dos pacientes nuestros desarrollaron necrosis tubular aguda. Luego de revisar la literatura hemos notado que prácticamente todos los casos de fallo renal agudo secundarios a Gentamicina usualmente estaban asociados al uso simultáneo de una Cephalosporina y raras veces ha ocurrido este fenómeno en pacientes cuya única terapia ha sido Gentamicina. Aparentemente el uso combinado de

estas drogas puede potenciar su nefrotoxicidad. Como posible mecanismo para explicar esto hemos postulado que Cephalothin puede desplazar la Gentamicina que existe ligada a proteína y que está en una forma inactiva. Al ocurrir esto se puede producir niveles altos de la forma activa de Gentamicina resultando en toxicidad renal. Se recomienda que aquellos pacientes que se traten con esta combinación de drogas se observen cuidadosamente para alteraciones tempranas en su función renal.

RENAL DYSFUNCTION ASSOCIATED WITH METHOXYFLURANE ANESTHESIA

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Reversible non-oliguric acute renal failure with hyponatremia-hyperosmolality may develop following anesthesia with methoxyflurane (Penthrane (R)). The incidence and degree of renal dysfunction associated with MOF anesthesia was prospectively studied in 15 adult volunteers with known renal function who were exposed to measured doses of MOF (n=10) or halothane (HALO) (n=5) anesthesia during elective uncomplicated surgical procedures. The maximum urine concentrating ability was markedly reduced (\downarrow 49 percent; $p < 0.001$) in all patients by day 2-3 after MOF (while remained unchanged after HALO anesthesia), and showed a partial recovery (of 20 percent from control) by day 5-10 after MOF. BUN, serum creatinine, glomerular filtration rate; serum electrolytes and osmolality were normal and remained unchanged after MOF. The defect in urine concentration was correlated with the extent of transformation of MOF to fluoride and oxalate rather than with duration of exposure and absorbed dose of MOF. An apparently reversible gross abnormality in maximal concentrating ability — the earliest evidence of nephrotoxicity — was revealed following MOF anesthesia in a group of patients challenged with water deprivation and exogenous vasopressin. Careful observation of renal functional changes and fluid balance should be done following MOF anesthesia.

UREMIC NONMALIGNANT HYPERTENSION: MECHANISMS AND TREATMENT

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Studies were undertaken in 11 normal subjects, 15 essential hypertension and 33 uremic patients to assess their cardiac hemodynamic pattern, plasma volume (PV), exchangeable sodium (Ex Na) and peripheral renin (PR) levels. Cardiac output, intraarterial blood pressure and peripheral vascular resistance index (PVRI) were measured. Mean cardiac index in 33 uremic patients (4.65 L/min/m^2) was higher ($p < 0.05$) than that of 11 normal volunteers (3.62 L/min/m^2) and 15 essential hypertension patients (3.32 L/min/m^2). Stroke index was not significantly different in normal (47.4 ml/beat/m^2), essential hypertension (46.3 ml/beat/m^2) and uremic (52.0 ml/beat/m^2) patients. However, the mean PVRI in hypertensive uremics was higher than normotensive uremics (2316 vs 1733 dynes/sec/cm⁻⁵/m²) with no difference in cardiac index, heart rate or stroke index. PV was significantly elevated in the hypertensive uremics when compared to normotensive uremics (2.39 vs 2.14 L/m^2) for the same level of hematocrit. PR levels were normal in all uremics (range 0 to 1.48 Goldblatt units $\times 10^{-4}$ /ml). Ex Na was elevated in all uremics but showed no difference between normotensive and hypertensive uremics. After chronic fluid removal with hemodialysis blood pressure of hypertensive uremics was controlled without the need of medication. Repeat studies showed the decrease in blood pressure was due to a decrease in PVRI accompanied by a decrease in PV, Ex Na and weight. These studies suggest uremic nonmalignant hypertension is hemodynamically sustained by an increase in PVRI rather than by an increased cardiac output. The renin angiotensin system does not appear to be related to the increased PVRI.

IMPORTANCE OF THE APPLICATION OF ELECTRON MICROSCOPY AND IMMUNO-FLUORESCENT MICROSCOPY TO THE STUDY OF KIDNEY DISEASES. Experience with 250 Renal Biopsies processed at the San Juan Veterans Administration Hospital.

Jesús M. Vázquez Urrutia, MD, Gustavo Ramírez de Arellano, MD, Osvaldo Ramírez Muxó, MD, José L. Cangiano, MD, Rafael Ramírez González, MD, and José Campos, MD. From the Electron Microscopy Unit of the Laboratory Service and Renal Dialysis Unit of the Medical Service of the San Juan Veterans Administration Hospital.

In recent years electron and immunofluorescent microscopy have added a new set of dimensions to the study of various disease states. Certainly the most important diagnostic contributions of these techniques have been in the study of kidney diseases. We have processed in our facilities approximately 250 renal biopsies including several interesting cases from the Puerto Rico Medical Center and Ponce District Hospital. Our experience with these biopsies has been quite rewarding from a number of view points:

1. It has stressed the importance of having a single centralized unit for the handling and processing of all the biopsy material so that from a single biopsy, material can be secured for light, electron and immunofluorescent studies.
2. In differentiating the immunologically mediated nephropathies from the non-immunologically mediated ones.
3. Differentiation of disease with similar clinical manifestation such as nephropathies associated with proteinuria or nephrotic syndrome.
4. Providing definite diagnosis in cases that could not otherwise be diagnosed, such as nephropathy associated with Goodpasture's syndrome, hereditary nephritis and IgA nephropathy.
5. As an aid in following patients with immunologically mediated types of glomerulonephritis being treated with drugs directed at the immunological mechanism involved.
6. Following glomerulonephritis with serial biopsies to determine its course so that appropriate therapeutic measures can be taken promptly when needed. Perhaps the most rewarding feature brought about by these new techniques is that by enhancing significantly our diagnostic capabilities in the study of renal diseases, appropriate measures are being taken to prevent progressive irreversible damage to the kidneys, hopefully preventing or at least delaying the appearance of some patients in chronic renal dialysis or kidney transplant programs.

INCIDENTAL RENAL SCANS IN PATIENTS UNDERGOING BRAIN SCANS WITH PER-TECHNETATE DTPA

A. L. Rodríguez-Rosado, MD and Julio V. Rivera, MD

Stannous diethylenetriaminepentaacetic acid (Tin-DTPA) labelled with technetium is an excellent agent for the scintigraphic exploration of the brain. Among the advantages of this agent are the achievements of higher

tumor to brain ratios and the sparing of the choroid plexus uptake effect without prior administration of blocking substances. Tin-DTPA is also suitable for renal imaging since it is rapidly excreted by the kidneys by glomerular filtration.

The purpose of this study was to do renal scanning incidental to the administration of a Tin-DTPA dose for brain scanning to determine the incidence of undiscovered renal pathology, anatomical variants and other unsuspected renal conditions in this group of patients.

We have studied 50 patients and discovered an incidence of unsuspected renal scintigraphic abnormalities which justified the routine incidental exploration of the kidneys in patients undergoing Tin-DTPA brain scanning.

*A. L. Rodríguez-Rosado, MD and Julio V. Rivera, MD.
From the Medical Nuclear Center and Hospital Pavia, Santurce.*

RENAL DYNAMIC STUDY (^{99m}Tc -DTPA) IN THE EVALUATION OF RENAL DISEASES

Julio V. Rivera, MD, A. L. Rodríguez-Rosado, MD and Justo González, MD. From the Medicine Department, Veterans Hospital.

When ^{99m}Tc DTPA is injected intravenously in the form of a bolus, its distribution in the renal arterial blood pool may be visualized by serial scintiphotography. As the radiopharmaceutical is excreted by glomerular filtration, its clearance into the collecting system occurs promptly and may also be followed. The efficacy of this procedure in the evaluation of various renal conditions, including renovascular disease and obstructive processes, has been studied in 30 patients. The correlation of this examination with other diagnostic procedures (intravenous pyelogram, arteriography) will be reviewed.

THE NEW DOCTRINE AS TO PHYSICIAN RESPONSIBILITY IN PUERTO RICO: THE MEANING OF THE OLIVEROS DECISION.

John L. Simon, MD, LLB

In February 1973, in the case of *Oliveros v. Abreu et al*, the Supreme Court of Puerto Rico revoked a juris-

prudential doctrine that had prevailed in Puerto Rico for over twenty years, although it really dated back to the 1880's in Massachusetts. The old rule, enunciated in Puerto Rico in *Rivera v. Dunscombe* (1952), had based the criterion for judging professional care in malpractice suits on the standards of practice in the community. The physician was only obliged to give to the patient such attention as was generally employed for similar cases by the other physicians in the community. The new test for judging physician performance, as announced by *Oliveros*, takes into account modern means of communication and teaching and establishes that the level or quality of care should be that which meets the standards generally recognized by the medical profession. The events leading up to the new decision, to what extent it represents a departure from the past, its meaning in practice, and its significance for the future are discussed.

CHEMOTHERAPY OF GASTROINTESTINAL CANCER-EXPERIENCE IN 100 PATIENTS.

Julio A. Morales-Rivera, MS IV, Antonio Grillo-López, MD, and Enrique Vélez-García, MD, Hematology Section, Department of Medicine, University of Puerto Rico School of Medicine.

One hundred patients treated with antineoplastic drugs for cancer of the gastrointestinal tract were evaluated to determine the effectiveness of chemotherapy in neoplastic disease of these sites. Histopathological classification was as follows: 98 adenocarcinomas (46 stomach, 25 colon, 12 rectum, 10 pancreas and 2 liver), 1 epidermoid carcinoma metastatic to pancreas and 1 hemangioendotheliosarcoma of liver. Fifty four patients underwent surgery as initial therapy, the remaining 46 had only palliative surgery or were ruled inoperable at time of diagnosis. Three patients received radiotherapy post-operatively. Ninety five patients received 5-fluorouracil as primary chemotherapy given intravenously in weekly doses, the other patients received other drugs. Drugs used were: vinblastine, methotrexate, 5-azacytidine, cyclophosphamide, two nitrosourea derivatives and thiotepe. Twelve patients had no evidence of disease at the start of chemotherapy but were treated because of the extent of disease found at surgery. Fifty four patients had some type of response, objective or subjective; of these, 22 had a measurable response. Thirteen of the 54 had liver or distant metastases and 8 of these had a measurable response. Thirty four of the 54 responders are alive and 28 are still on chemotherapy. Of the 46 who did

not respond, 28 had liver or distant metastases; 11 are alive and 8 are still on chemotherapy. Forty three patients had some evidence of toxicity, none so severe to force discontinuation of therapy. A review of the current status of chemotherapy in gastrointestinal malignancies will be made.

COMBINATION CHEMOTHERAPY FOR DISSEMINATED CARCINOMA OF THE BREAST.

José A. Lozada, MD, Antonio J. Grillo-López, MD and Enrique Vélez-García, MD, Hematology Section, Department of Medicine, University of Puerto Rico School of Medicine.

Disseminated carcinoma of the breast with or without previous treatment with surgery or radiotherapy has been considered until recently, a situation in which little could be offered to the patient short of analgesia and other supportive measures. During the last decade various drugs have been shown useful in the palliation of this neoplasm. We are herewith reporting our experience with 100 cases of disseminated breast carcinoma treated with various combinations of the following drugs: 5-fluorouracil, vincristine, methotrexate, thiotepe, cyclophosphamide and prednisone. Significant objective remissions were obtained in a considerable number of patients. It is our belief that these results are optimistic from the standpoint of improving survival and quality of life. Toxicity and side effects although existent, were moderate enough to allow complete courses of therapy safely and with minor complications. The use of drug combinations earlier in the course of this disease may lead the way to better therapeutic results in the future.

EVALUATION OF CONTINUOUS 5-FLUOROURACIL (5-FU) INFUSION IN CANCER THERAPY

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5-FU is considered the cornerstone of gastrointestinal (GI) cancer chemotherapy. However, its optimal dosage, method of administration, and tumor spectrum remain to be firmly established. The traditional loading dose method followed by maintenance doses IV every other day until toxicity, produces objective tumor regressions in about 20 percent of patients with GI cancer. It has also produced significant related mortality. To this date, the package insert still advocates

this obsolete and dangerous regimen. Recently, the IV single dose, weekly regimen has been shown to produce similar clinical response with far less toxicity and no mortality. This study was designed to explore another method of 5-FU administration, to determine its tumor spectrum and toxicity, and to evaluate clinical responses, particularly in patients with GI cancer. Twenty patients with far advanced disease received continuous 5 day infusions of 5-FU which were repeated every 21 days. Subjective improvement was attained in patients with tumors of: Pancreas (1/4); Stomach (3/4); Colon (5/9); and Lung (1/1). Objective regressions occurred in the following tumors: Stomach (2/4); Pancreas (1/4); Colon (3/9); and Lung (1/1). Toxicity was minimal despite the massive doses of 5-FU utilized. There was one episode of severe oropharyngeal mucositis with recovery occurring within two weeks, and 3 episodes of moderate hematologic toxicity in patients with sepsis. The response obtained in these patients, many of whom had received 5-FU by other methods, is encouraging. The continuous 5 day infusion method certainly merits further evaluation in patients with earlier stages of disease and who have not been subjected to previous chemotherapy.

LA GAMAGRAFIA CON ^{67}Ga EN EL ESTUDIO DE PACIENTES CON LINFOMAS

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Habiéndose publicado que el ^{67}Ga muestra selectividad de fijación por los linfomas, se ha preconizado su uso para localización de este tipo de tumores, agregándose además así una forma no traumática de establecer estadio de la enfermedad en algunos casos.

Se utilizó ^{67}Ga endovenoso, en forma de citrato, para el estudio de 20 pacientes con diagnóstico de diferentes tipos de linfomas en la Cámara de Anger y en el Gamagrafo de Cuerpo Entero. En general se obtuvo una buena visualización de las lesiones conocidas y se observaron otras que eran insospechadas.

Se analizan algunas imágenes obtenidas en los pacientes estudiados.

Se concluye que el nuevo método puede ser de gran ayuda en el diagnóstico y seguimiento de pacientes con linfomas.

ESTIMULACION ANTIGENICA DE LINFOCI-

TOS POR CELULAS MALIGNAS DE LINFOMA: EVIDENCIA DE UN NUEVO ANTIGENO TUMORAL

Fernando Cabanillas, MD, Marisel Roque, BS, MT y Francisco Muñoz, MD.

Recientemente se ha descrito la existencia de sustancias antigénicas en varios tipos de tumores. En el grupo de los linfomas solo existe evidencia en este sentido para el mal de Hodgkin. Hemos tenido la oportunidad de separar los leucocitos periféricos de un paciente con linfoma maligno de tipo mixto en fase leucémica. Se usaron dos métodos de separación: 1) Ficoll-Hypaque que utiliza diferencias en densidad celular y 2) un retículo de nylon que retiene las células fagocíticas. El primer método permitió obtener una colonia mixta que consistía de linfocitos morfológicamente normales además de células linfomatosas que tenían propiedades fagocíticas. Con el segundo método se obtuvo una colonia prácticamente pura de linfocitos morfológicamente normales. El grado de transformación blástica de los linfocitos según se mide por la incorporación de timidina tritiada fue utilizado como índice de estimulación antigénica. Se observó que la colonia mixta exhibía una transformación catorce veces mayor que la colonia de linfocitos normales. A la luz de estos resultados y de los controles, se cree que la explicación más lógica para este fenómeno es que las células linfomatosas poseen un antígeno tumoral capaz de servir como estímulo para transformación de los linfocitos normales en células blásticas.

IMMUNOLOGIC STUDIES IN HUMANS WITH SCHISTOSOMIASIS MANSONI

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Sera was obtained from 26 humans with schistosomiasis mansoni and analyzed for the presence of precipitating antibodies to *S. mansoni* cercarial, adult worm, and egg antigenic extracts as well as for the presence of circulating schistosome antigens using sera from rabbits hyperimmunized against each of the three antigenic extracts. The number of *S. mansoni* eggs per gram of feces excreted by each of these individuals was determined quantitatively and ranged from 1 to 2,483 eggs per gram.

Using Ouchterlony double diffusion analysis, the

results show that 24 of 26 serum samples reacted to at least one antigenic extract demonstrating the presence of precipitating antibodies. These sera reacted most frequently and strongly with egg extract although no correlation could be demonstrated between reactivity and the number of eggs being excreted by the same individual. More significant was the observation that 9 of 16 serum samples had at least one circulating parasite antigen, presumably in immune complex form, with adult worm circulating antigen predominating. Although no correlations between egg excretion and circulating antigen could be observed, the results are of special interest in view of recent theories concerning immune complex nephritis in man and experimental animals infected with schistosomiasis.

This is the first demonstration of circulating schistosome antigen in the serum of humans infected with schistosomiasis mansoni.

SCHISTOSOMA MANSONI — Radiological Manifestations

Heriberto Pagán Sáez, MD. From the UPR School of Medicine and Puerto Rico Medical Center.

The complex life cycle of *Schistosoma mansoni* gives rise to varied clinical and pathological manifestations. The radiographical manifestations are a reflection of the anatomopathological changes caused by the reaction of the host tissues with the different stages of the parasite in its voyage through the vascular system. The parasite makes its entrance through the skin passing into the vascular system via the lymphatics and eventually reaches the intrahepatic portal veins where the worm matures. The blood fluke migrates against the portal current into the mesenteric veins where oviposition takes place.

The egg is the causative agent of the chronic phase of the disease. The reactions between the tissue of the host with the egg and its products leads to the characteristic lesions found throughout the human host.

The radiological findings can be summarized as follows:

- A. In the Acute or Toxemic Form
 1. Disseminated miliary or nodular pulmonary infiltrates
- B. In the Chronic Form
 1. Hepatosplenic (Portal Hypertension Syndrome)

2. Cardiopulmonary
 - a. Pulmonary Arterial Hypertension Syndrome
 - b. Pulmonary Cyanotic Syndrome
3. Intestinal Granulomata
4. Retroperitoneal Granulomata
5. Central Nervous System Granulomata

ENTEROPATHOGENIC INTESTINAL BACTERIA IN TROPICAL SPRUE.

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Culture of fasting and postprandial midjejunal aspirates using both aerobic and strict anaerobic techniques produced growth in samples from 10 to 11 patients with untreated tropical sprue, 2 of 4 healthy North Americans, and 7 of 9 randomly selected Puerto Rican control subjects, 2 of whom had diarrhea and one of whom had malabsorption. Viable bacteria were more numerous in the sprue patient; their predominant intestinal flora consisted of facultative aerobic coliforms (*Klebsiella pneumoniae* in 7, *Enterobacter cloacae* in 2, *Escherichia coli* in one). Every type of the predominant coliforms present in each of the 10 sprue patients with bacterial growth elaborated an enterotoxin which produced net secretion in the rabbit ileal loop model. The principal fermentation product of these bacteria, ethanol, was present in the aspirates from 8 of 9 sprue patients tested. Both symptomatic Puerto Rican control subjects also harbored similar types of coliforms some, but not all, of which elaborated an enterotoxin, and ethanol was present in the aspirate of the one subject tested. In contrast, the jejunal flora of the asymptomatic Puerto Ricans and the North Americans consisted, with one exception, exclusively of either aerobic gram-positive or obligately anaerobic bacteria and none of these subjects either had alcohol in their aspirate or harbored a bacteria that elaborated an enterotoxin. These observations demonstrate that the mid-jejunal flora of patients with tropical sprue differs from that of healthy persons living either in temperate or tropical areas in that it is populated by coliform organisms which elaborate substances that alter intestinal function.

PARABIOTIC PERFUSION AND DIALYSIS IN EXPERIMENTAL HEPATIC COMA

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Most models of hepatic coma simulate a subacute or chronic liver damage with chronic failure and hyperammonemia, but not the massively necrotic liver which we see in some forms of fulminant hepatitis. To simulate this situation, mongrel dogs underwent *en-bloc* ligation of the portal triad and gastrohepatic omentum after a decompressing side-to-side portacaval shunt. In spite of antibiotics, steroids, and correction of hypovolemia and acidosis, 12/12 dogs invariably developed progressive coma in 4-12 hrs. (mean 7 hrs.) and died in 8-18 hrs. (mean 12 hrs.). Postmortem examination showed necrotic liver and hemorrhagic ascites.

Direct cross-circulation performed against healthy dogs resulted in brief lightening of coma and survival for 34, 35, 36 hours (3 dogs). The healthy "donor" dogs promptly lapsed into coma and usually died after 10-16 hours of cross-circulation. When this occurred, a second healthy dog was put in its place. Cross-dialysis was performed across membranes of varying pore-size and transfer capacity. Cuprophane (M.W. 15,000) and Amicon PM-30 (M.W. 30,000) failed to revert coma in any dog, and prolonged survival to 20 hours in only one dog (9, 12, 13, 15, 14, 20 hrs.). Union Carbide membrane (M.W. approx. 100,000) lightened coma in two 24 hrs. survivors (12, 12, 24, 24 hrs.). Donor dogs suffered a similar fate.

This model results in reproducible massive liver necrosis, with progressive failure and coma. Cross perfusion and cross dialysis with large-pore membranes may prolong may survival and temporarily improve the coma.

ENFERMEDAD HEPATICA EN DONANTES POSITIVOS PARA EL ANTIGENO DE LA HEPATITIS B

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El 29 de abril de 1971 se comenzó en el Banco de Sangre de la Cruz Roja de San Juan, Puerto Rico, a estudiar sistemáticamente los donantes de sangre para determinar si el antígeno de la Hepatitis B estaba presente

en ellos. De esta fecha al 31 de diciembre de 1971 se estudiaron 9,520 donantes asintomáticos de los cuales 35 o sea 0.36 por ciento resultaron positivos. De estos pacientes se pudieron estudiar detenidamente treinta y uno, practicándoles a todos una biopsia hepática así como estudios repetidos de la función de este órgano. Se estudió además la microscopía electrónica para partículas Dane y sub-tipificación *ay* y *ad*.

En tres de los treinta y un pacientes el patólogo encontró que el tejido no era suficiente para un diagnóstico definitivo, en los veintiocho restantes la patología encontrada fue como sigue:

Histología normal — 9
Hígado graso — 5
Granulomas — 5
Hepatitis crónica persistente — 2
Cirrosis inactiva — 1
Cirrosis activa — 2
Hepatitis crónica activa — 4

Estos datos reflejan la alta incidencia (32 por ciento) de enfermedad hepática potencialmente relacionada a una infección asintomática con el virus de la hepatitis B.

Se discutirán las relaciones entre los diferentes diagnósticos y la presencia de los distintos sub tipos y partículas en el suero de estos pacientes.

ULTRAESTRUCTURA EN LA "INDUCED ATROPHIC GASTRITIS FOR THE TREATMENT OF PEPTIC ULCER"

A. Rodríguez Olleros, MD, J. E. Taveras, MD, E. Febles Vizcarrondo and A. Martínez Palomo, MD

A study of the biopsies of the seven patients treated with our method was performed before and after treatment with the electronic microscope. The study of the ultrastructure was focused on the parietal and principal cells of the gastric glands. Our observations were the following: 1. Some alterations are evident in the gastric gland of the several specimens of our study. They are rather moderate and are noted both in the parietal and principal cells; 2. Alterations in the principal cells are compatible with cellular degeneration: ie: picnosis, pronounced dilatation of the endoplasmic reticulum and moderate accumulations of dense bodies. Next to the principle cells that show these alterations are numerous cells of the same type do not show appreciable structural changes; 3. In a large portion of the parietal cells from the atrophic material there can be observed numerous clumps of residual bodies, myelin-

like figures and lisosomas compatible with licalized degenerative cytoplasm changes; 4. In some parietal cells we find dilatation of the inter and extracellular canaliculi in which there is probably a loss of microvilli; 5. In the atrophic material there exists a reasonable portion of parietal cells with normal ultrastructure.

TREATMENT OF SOFT TISSUE INJURIES
IN MAXILLOFACIAL TRAUMA

Miguel R. Alonso, MD, Ashford Medical Center 603, San-
turce, Puerto Rico.

Cheek wounds, with minor tissue losses, are easily approximated after the skin is undermined and relaxa-
tion incisions made to reduce tension. Whenever pos-
sible, these closures are made to fit into the lines of
facial expression. Larger losses of skin require local
flaps. The rotation flap is the simplest and most fre-
quently employed technique. In cases where it appears
that a flap would distort the eyelids, lips, or nose, a split
thickness skin graft is considered to prevent contracture
in anticipating the need for a future reconstructive pro-
cedure. For similar reasons, full thickness defects into
the oral cavity or lip are closed by suturing oral mucosa
to skin. Partially avulsed pedicles with apparent signifi-
cant discoloration in the periphery, can be saved with
minimal debridement when the base has a good color.

TRANSTHORACIC ELECTRICAL IMPEDAN-
CE AS A CLINICAL GUIDE OF PULMONARY
FLUID ACCUMULATION IN CONGESTIVE
HEART FAILURE

Marcos U. Ramos, MD, (by invitation), John W. LaBree, MD,
and William G. Kubicek, PhD (by invitation).

Involvement in the field of Cardiac Rehabilitation
requires the understanding of clinical conditions which
may interfere with the patient's program. Most clini-
cians are aware of the difficulty in evaluating quantita-
tively the severity and the extent of the pulmonary
congestion and edema resulting from heart failure.
The changes in transthoracic electrical impedance have
been found to correlate linearly with the intrathoracic
fluid volume.

Three patients, in whom the diagnosis of congestive
heart failure was made, were studied using the Minnesota
impedance cardiograph described by Kubicek and asso-
ciates. This method offers the advantage of being non-

invasive and easily repeatable.

Serial impedance measurements were recorded in
supine position during their clinical course. In two of
the patients who eventually recovered, the transthoracic
electrical impedance reading showed a recovery toward
normal values even prior to a clinically detectable
improvement. In the third patient, who eventually
died, the transthoracic electrical impedance continued
decreasing in spite of diuretic therapy and adequate
diuresis.

Correlation of the weight loss due to diuresis and
the change in impedance shows that the intrathoracic
fluid volume changes 24 to 48 hours after the
diuresis. Possible explanations for this phenomenon
will be discussed.

COMPARISON OF MINNESOTA IMPEDAN-
CE CARDIOGRAPH AND ELECTROCARDIO-
GRAPH IN BICYCLE STRESS TESTING IN
EARLY POST MYOCARDIAL INFARCTION
PATIENTS

Marcos Ramos, MD, John LaBree, MD, W. Remole, MD,
W. G. Kubicek, MD and F. J. Kottke, MD. Medical School,
University of Minn., Mpls., Minn.

Bicycle ergometer stress tests were performed on 55
patients within the first 3 weeks after myocardial
infarction (MI) or acute ischemia was diagnosed. They
were monitored with a multilead ECG and the Minne-
sota Impedance Cardiograph (ZCG) before, during and
after 6 minutes of exercise. Analysis of ECG and ZCG
results revealed a poor correlation between the ischemic
changes as indicated by the ECG and the cardiac output
and contractility responses obtained by the ZCG. ECG
was graded according to millimeters (S-T) segment
deviation. ZCG was graded from a normal output
response (A) to no or falling response (D). Example, 8
patients data are shown in square DO indicating a very
poor output response with a normal ECG. The ZCG
provided reliable data in all cases regarding ability
of the damaged heart to respond to exercise stress
while the ECG correlated only in the shaded area of
table. Clinical observations confirmed the ZCG data.

		ECG			
		0	1	2	3
ZCG	A	5	8	2	0
	B	5	10	1	2
	C	1	3	1	2
	D	8	6	0	1

THE ROLE OF SELECTIVE CORONARY ARTERIOGRAPHY IN THE MANAGEMENT OF CHEST PAIN

José A. Pereyó, MD, Esteban Linares-Rivera, MD and Eli A. Ramírez, MD, MS, FACP.

Sixty three patients were studied by selective coronary arteriography in whom coronary artery disease was known or suspected on a clinical basis. The clinical data is analyzed and correlated with the coronary arteriography findings. The history, physical examination, electro and roentgenographic findings, serum lipids, vectocardiogram and exercise stress test, among others, are analyzed. Of these, only the stress test correlated closely with the presence of coronary artery disease demonstrated by arteriography. Serum lipids were more frequently elevated in patients with abnormal arteriograms.

Five patients with positive stress test who had normal arteriograms will be discussed. Three patients with chest pains and abnormal electrocardiograms were found to have incipient idiopathic hypertrophic sub-aortic stenosis and normal arteriograms. Five patients with atypical chest pain and negative stress test had normal arteriograms.

Coronary arteriography is indicated in patients evaluated for coronary artery bypass surgery or aortic valvular surgery and in patients with chest pain or non specific electrocardiographic changes that have been attributed to the presence of coronary artery disease.

THE EFFECT OF SPREAD OF EXCITATION ON THE CARDIOVASCULAR SYSTEM DURING PROLONGED ISOMETRIC EXERCISE

Marcos U. Ramos, MD, Martin O. Mundale, MS, Essam A. Awad, MD, PhD, Theodore M. Cole, MD, David A. Witsoe, MS, EE, Mildred Olson, BS, MT and Frederic J. Kottke, MD, PhD.

Isometric exercise during convalescence following myocardial infarction has been reported to be potentially dangerous. The severity of the resultant hemodynamic changes did not appear to relate to the size of the isometrically exercised muscle group. This investigation studied the effect of spread of muscular recruitment on the cardiovascular system during prolonged isometric exercise at six levels of intensity of effort in six normal subjects. Recruitment to eight different muscles, grip strength, mean arterial blood

pressure and heart and respiratory rates were recorded simultaneously. The results indicated a significant correlation between the increase in the cardiac parameters and the increase in muscular recruitment. The increase in the musculoskeletal and cardiovascular parameters varied directly with the percent level of exercise, the temporal progression of the exercise bouts and with the volitional effort to maintain a predetermined level of motor activity.

Cortical effort to maintain a sustained and precise predetermined level of motor activity causes progressive expansion of neuronal activation of the somatic and vasomotor centers. It appears that both the progressive muscle recruitment and cardiovascular changes are the peripheral expression of a central excitatory process rather than a pressor reflex chemically or hormonally mediated.

PhD. From the Department of Physical Medicine and Rehabilitation, University of Minnesota Medical School, Minneapolis, Minnesota.

ACCELERATED IDIOVENTRICULAR RHYTHM DURING PREGNANCY: A REPORT OF TWO CASES

Juan M. Aranda, MD and Francisco Veray, MD. From the Department of Medicine, University District Hospital, University of Puerto Rico School of Medicine and the Department of Medicine, Beach Army Hospital, Fort Wolters, Texas.

Accelerated idioventricular rhythm was first noted after experimental coronary occlusion and has subsequently been reported with various terminologies; slow ventricular tachycardia, nonparoxysmal ventricular tachycardia, accelerated ventricular rhythm, idioventricular tachycardia and accelerated isorhythmic ventricular rhythms. The arrhythmia has been reported in association with acute myocardial infarction, digitalis toxicity, rheumatic heart disease, myocardiopathy and rarely in pregnant women without evidence of heart disease. The clinical significance of this rhythm during pregnancy is incompletely understood at this time, since not many cases have been reported in the literature. Two cases of accelerated idioventricular rhythm during pregnancy are presented with special emphasis on the benign nature of the arrhythmia due primarily to the isorhythmic discharge rate which made paroxysmal emergence and appearance in the vulnerable period unlikely. The clinical experience in the cases associated

with acute myocardial infarction and digitalis toxicity suggest that the arrhythmia is relatively benign and usually requires no treatment.

DETERMINACION DE LA PERFUSION PULMONAR EN LA TETRALOGIA DE FALLOT, MEDIANTE LA GAMAGRAFIA

René C. Dietrich, MD, Jorge Sánchez, MD, Aldo Lanaro, MD y A. Martínez Picó, MD. Del Centro Nuclear de P. R., Centro Médico, Río Piedras, P. R.

La Tetralogía de Fallot es la anomalía congénita cianótica más frecuente, presentando variaciones en el flujo pulmonar que se pueden determinar mediante la gamagrafía.

Se realizaron 44 gamagrafías en 40 pacientes con Tetralogía comprobadas por cateterismo cardíaco. Los

resultados se clasifican en tres grupos:

Grupo I — Pacientes que no tuvieron cirugía y el flujo es uniformemente deficiente en ambos pulmones.

Grupo II — Pacientes que tuvieron cirugía paliativa existiendo marcada asimetría en la distribución del flujo pulmonar.

Grupo III — Pacientes con corrección quirúrgica total y con normalidad en la perfusión o disminución segmental.

El presente estudio permite juzgar el grado de estenosis pulmonar, los resultados de la cirugía paliativa, la integridad vascular previa a la cirugía y el retorno a la normalidad después de la corrección total. La sencillez, baja exposición de radiación y ausencia de peligro para el paciente hacen de este método el más apropiado para la evaluación de estos pacientes.

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Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired. Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (> 5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities. Accordingly, check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently—both can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides

are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in postsympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with anti-hypertensive agents may result in an additive hypotensive effect.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Rarely, necrotizing vasculitis, paresthesias, icterus, pancreatitis, and xanthopsia have occurred with thiazides alone.

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```

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Actions—Ovulen and Demulen act to prevent ovulation by inhibiting the output of gonadotropins from the pituitary gland. Ovulen and Demulen depress the output of both the follicle-stimulating hormone (FSH) and the luteinizing hormone (LH).

Special note—Oral contraceptives have been marketed in the United States since 1960. Reported pregnancy rates vary from product to product. The effectiveness of the sequential products appears to be somewhat lower than that of the combination products. Both types provide almost completely effective contraception.

An increased risk of thromboembolic disease associated with the use of hormonal contraceptives has now been shown in studies conducted in both Great Britain and the United States. Other risks, such as those of elevated blood pressure, liver disease and reduced tolerance to carbohydrates, have not been quantitated with precision.

Long-term administration of both natural and synthetic estrogens in subprimate animal species in multiples of the human dose increases the frequency of some animal carcinomas. These data cannot be transposed directly to man. The possible carcinogenicity due to the estrogens can be neither affirmed nor refuted at this time. Close clinical surveillance of all women taking oral contraceptives must be continued.

Indication—Ovulen and Demulen are indicated for oral contraception.

Contraindications—Patients with thrombophlebitis, thromboembolic disorders, cerebral apoplexy or a past history of these conditions, markedly impaired liver function, known or suspected carcinoma of the breast, known or suspected estrogen-dependent neoplasia and undiagnosed abnormal genital bleeding.

Warnings—The physician should be alert to the earliest manifestations of thrombotic disorders (thrombophlebitis, cerebrovascular disorders, pulmonary embolism and retinal thrombosis). Should any of these occur or be suspected the drug should be discontinued immediately.

Retrospective studies of morbidity and mortality conducted in Great Britain and studies of morbidity in the United States have shown a statistically significant association between thrombophlebitis, pulmonary embolism, and cerebral thrombosis and embolism and the use of oral contraceptives. There have been three principal studies in Britain¹⁻³ leading to this conclusion, and one⁴ in the United States. The estimate of the relative risk of thromboembolism in the study by Vessey and Doll³ was about sevenfold, while Sartwell and associates⁴ in the United States found a relative risk of 4.4, meaning that the users are several times as likely to undergo thromboembolic disease without evident cause as non-users. The American study also indicated that the risk did not persist after discontinuation of administration and that it was not enhanced by long-continued administration. The American study was not designed to evaluate a difference between products. However, the study suggested that there might be an increased risk of thromboembolic disease in users of sequential products. This risk cannot be quantitated, and further studies to confirm this finding are desirable.

Discontinue medication pending examination if there is sudden partial or complete loss of vision, or if there is a sudden onset of proptosis, diplopia or migraine. If examination reveals papilledema or retinal vascular lesions medication should be withdrawn.

Since the safety of Ovulen and Demulen in pregnancy has not been demonstrated, it is recommended that for any patient who has missed two consecutive periods pregnancy should be ruled out before continuing the contraceptive regimen. If the patient has not adhered to the prescribed schedule the possibility of pregnancy should be considered at the time of the first missed period.

A small fraction of the hormonal agents in oral contraceptives has been identified in the milk of mothers receiving these drugs. The long-range effect to the nursing infant cannot be determined at this time.

Precautions—The pretreatment and periodic physical examinations should include special reference to the breasts and pelvic organs, including a Papanicolaou smear since estrogens have been known to produce tumors, some of them malignant, in five species of subprimate animals. Endocrine and possibly liver function tests may be affected by treatment with Ovulen or Demulen. Therefore, if such tests are abnormal in a patient taking Ovulen or Demulen, it is recommended that they be repeated after the drug has been withdrawn for two months. Under the influence of progestogen-estrogen preparations preexisting uterine fibromyomas may increase in size. Because these agents may cause some degree of

fluid retention, conditions which might be influenced by this factor, such as epilepsy, migraine, asthma, cardiac or renal dysfunction, require careful observation. In breakthrough bleeding, and in all cases of irregular bleeding per vaginam, nonfunctional causes should be borne in mind. In undiagnosed bleeding per vaginam adequate diagnostic measures are indicated. Patients with a history of psychic depression should be carefully observed and the drug discontinued if the depression recurs to a serious degree. Any possible influence of prolonged Ovulen or Demulen therapy on pituitary, ovarian, adrenal, hepatic or uterine function awaits further study. A decrease in glucose tolerance has been observed in a significant percentage of patients on oral contraceptives. The mechanism of this decrease is obscure. For this reason, diabetic patients should be carefully observed while receiving Ovulen or Demulen therapy. The age of the patient constitutes no absolute limiting factor, although treatment with Ovulen or Demulen may mask the onset of the climacteric. The pathologist should be advised of Ovulen or Demulen therapy when relevant specimens are submitted. Susceptible women may experience an increase in blood pressure following administration of contraceptive steroids.

Adverse reactions observed in patients receiving oral contraceptives—A statistically significant association has been demonstrated between use of oral contraceptives and the following serious adverse reactions: thrombophlebitis, pulmonary embolism and cerebral thrombosis.

Although available evidence is suggestive of an association, such a relationship has been neither confirmed nor refuted for the following serious adverse reactions: neuro-ocular lesions, e.g., retinal thrombosis and optic neuritis.

The following adverse reactions are known to occur in patients receiving oral contraceptives: nausea, vomiting, gastrointestinal symptoms (such as abdominal cramps and bloating), breakthrough bleeding, spotting, change in menstrual flow, amenorrhea during and after treatment, edema, chloasma or melasma, breast changes (tenderness, enlargement and secretion), change in weight (increase or decrease), changes in cervical erosion and cervical secretions, suppression of lactation when given immediately post partum, cholestatic jaundice, migraine, rash (allergic), rise in blood pressure in susceptible individuals and mental depression.

Although the following adverse reactions have been reported in users of oral contraceptives, an association has been neither confirmed nor refuted: anovulation post treatment, premenstrual-like syndrome, changes in libido, changes in appetite, cystitis-like syndrome, headache, nervousness, dizziness, fatigue, backache, hirsutism, loss of scalp hair, erythema multiforme, erythema nodosum, hemorrhagic eruption and itching.

The following laboratory results may be altered by the use of oral contraceptives: hepatic function: increased sulfobromophthalein retention and other tests; coagulation tests: increase in prothrombin, Factors VII, VIII, IX and X; thyroid function: increase in PBI and butanol extractable protein bound iodine, and decrease in T₃ uptake values; metyrapone test and pregnanediol determination.

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CORONARY ARTERIOGRAPHY: A REVIEW (SECOND PART)

Charles D. Johnson, MD, FACP, FACC

Complications

Coronary arteriography is a relative safe procedure (92). The complications are those of cardiac catheterization and angiography in general: allergic reactions, pyrogenic reactions, hemorrhage, vagal reactions, hypotension, radiation, pain in arm or leg, pseudoaneurysm formation, LV dysfunction due to the contrast agent, transient arrhythmias, along with rare special complications (93, 94). Brachial artery occlusion has been encountered in 1-7 percent of cases. The use of Fogarty catheters have been valuable; vascular complications may require prompt surgical evaluation and treatment (95). Sinus bradycardia is to be anticipated but may be managed by requesting the patient to cough forcefully just after the injection. Ventricular fibrillation may occur in about 0.75 percent (0.5-2 percent) of cases, (stated to be rare with the use of meglumine diatrizoate Renografin 76) but the procedure can usually be continued after defibrillation. Dissection of a coronary artery or atherosclerotic plaque has been rarely documented (96). An acute MI has occurred rarely (0.3-2.6 percent-several with normal coronary arteries). Only 12 MI's in 21,000 studies occurred in Sones' laboratory. Coronary spasm may be a factor (97). However, in a population of patients with severe CAD the incidence of MI occurring during the waiting period prior to the study will exceed that due to the procedure (98). Overall nonlethal complications have occurred in about 2 percent of cases. Mortality is extremely rare (0.1-0.6 percent). In Sones' laboratory there has been 20 deaths in 22,600 cine coronary arteriograms (<0.1 percent) (75). Judkins had 2 deaths in 4500 studies (99). Gensini had none in his last 1500 cases (50). But as just recently emphasized by Selzer and associates, these low statistics may not prevail in "low volume" institutions where arterial occlusions, complications and death may be many fold higher (45,100). Mortality may reach 8 percent with

the first 25 cases; after a training and experience period of 700-800 cases, the mortality is extremely low. Thromboembolism, spasm of an artery, cardiac arrest, cerebrovascular accidents, median nerve injury, are other rare complications (101, 102).

So, the procedure is not to be approached by the casual catheterizer. Constant monitoring and facilities for defibrillation and resuscitation are necessary. Preventive guide lines have been published (99).

Errors

Errors can be committed in the performance and interpretation of this specialized test (29, 44, 103). End-on vessels, small arteries obstructed flush with the parent vessel, twig occlusion, spasm of an artery, layering of contrast material and myocardial bridges may be misinterpreted. NG is necessary to dilate the arteries, to exclude spasm and to demonstrate silent lesions, minimal lesions and collaterals (104); multiple oblique films are mandatory. Luminal narrowings of 25 percent or less may not be detected, or even more severe degrees of narrowing if these are circumferential, cylindrical or smooth (3, 36). However, small radicals and intercoronary collaterals of 100-200u should be defined (13). In general, CA underestimates the severity of the disease (3, 20). The false negative rate may be <2 percent and the false positive rate near zero. If technical factors are compromised, errors increase.

Several types of possible errors have been pointed-out by Sheldon (49): failure to identify an anterior descending (AD) branch of the left coronary artery (LCA), which may be obstructed or which may uncommonly arise ectopically from the right coronary artery (RCA). Apparent narrowing of the proximal portion of a coronary artery at the tip of the catheter may be due to functional constriction from mechanical stimulation of the catheter rather than segmental stenosis of atherosclerosis. Certain areas are difficult to visualize, requiring close examination-the orifices of the right and left coronaries, the bifurcation of the

left main trunk, the proximal segments of the AD, left circumflex and main trunk, and the origins of the diagonal branches of the AD, which may be obstructed flush with the AD and thus be missed (look for collaterals). Mild focal impairment of LV contractility may be mis-interpreted as irreversible myocardial damage and fibrous replacement; ischemia without fibrosis may cause an abnormal ventriculographic response. Isoproterenol and amyl nitrite may distinguish the functional impaired LV from that of interstitial fibrosis.

Limitations consist of those due to radiologic technique, resolution, filming, inconstant anatomic patterns of minor vessels and opacification of small vessels (47). Angiography underestimates the degree of narrowing, and does not always correlate well with the gross and microscopic changes of the coronary arteries; a slide-like lumen adjacent to the atheroma may be an additional factor (105).

Correlations

There is a high correlation of the results of CA and the clinical diagnoses of a definite MI (over 98 percent), AP (about 90 percent) and in patients thought to be free of CAD (over 95 percent). In patients with a possible MI, only 74 percent had significant findings, in atypical AP only about 65 percent, while rest pain, coronary failure and congestive failure demonstrated significant obstruction in about 79, 79 and 87 percent of cases, respectively. Seventeen percent not considered to have CHD, demonstrated significant abnormalities. Almost all the patients had been told by physicians that coronary disease was present or suspected, but about 37 percent had no significant obstruction and over 27 percent had normal arteriograms (28). A recent study revealed good clinical correlation: all patients with severe arterial lesions had typical angina, and the longer the duration of the AP the greater the extent of disease. The ECG also correlated well in that 79 percent of resting ECG's of patients with CAD were abnormal with prior infarction in 36 percent (106).

Clinical symptoms are usually, but not always, associated with occlusive disease involving at least two major coronary arteries. Diffuse disease is usually present when symptoms first appear. An infarct pattern by the ECG is usually associated with significant obstructive disease of at least one major artery (40). There may be similar arteriographic lesions in patients with AP and MI, except for differences in collaterals, rudimentary vessels and focal bridging (107).

Coronary constrictions of 75-80 percent or more are important, while usually those less than 50 percent do not cause symptoms or lead to complications. A single mild obstructive lesion uncommonly causes anginal symptoms (105), perhaps when associated with other disease. There may be a poor correlation between the extent of anatomic CAD and the functional significance of the disease.

Typical AP and MI, alone or together, usually indicate multivessel involvement. One series showed involvement of only one vessel in 23 percent of cases. A remote MI by the ECG usually means CAD. The electrocardiographic location of the infarction may be valuable in predicting the sites of coronary arterial obstruction and ventricular asynergy in transmural MI. It is impossible to predict with any certainty the angiographic changes on the basis of the duration, location or severity of symptoms, although with only a single lesion symptoms will likely be of short duration (108). Overall, there is a relationship between lipid and carbohydrate abnormalities, and angiographic abnormalities.

So, in 4 studies a history of typical AP was an excellent indicator of CAD, revealing positive arteriograms in about 90 percent of cases. But positive arteriograms were present in only 23-66 percent of cases with atypical angina and in only 4-17 percent of cases without ischemic pain (108).

Resting ECG's are quite insensitive and nonspecific for diagnosing CAD, and in the opinion of some the Single and Double Master's Tests are likewise insensitive. Exercise stress, such as graded treadmill exercise, increases the diagnostic sensitivity and specificity (a positive ST response has been noted in 82 percent of patients with AP). As a group, patients with AP and ST-abnormalities, have a high prevalence of CAD, but sensitivity is poor for the individual patient (108). There may be a rough correlation between the degree of LV dysfunction and the extent of coronary disease, especially if exercise and pacing stress is utilized (109). The submaximal treadmill stress test does not predict the location of CAD and is more likely to be negative in disease limited to a single vessel (110). Using graded exercise the incidence of positive tests increased with the increasing severity and extent of CAD (61 percent of patients with single vessel and 93 percent with 2-or 3-vessel disease had positive ST segment responses). A normal response in a patient with AP and CAD, suggests isolated disease of the RCA or left coronary system (111). (112, 113, 114, 115).

A recent study found frequently severe coronary disease in patients with highly atypical chest sensations,

and fairly normal arteries in patients with quite significant histories of chest pain (52). In their 110 cases with chest pain, of 35 cases with classical AP, 31 had CAD (90 percent or greater), 3 had IHSS and 1 congestive cardiomyopathy. Of 17 patients with atypical pain, 5 had CAD (one-third), and the rest had normal arteries or no significant disease. Of 58 patients with previous MI's, all demonstrated significant CAD. Nocturnal AP has occurred with disease of a single coronary artery (116). *The patient with chest pains attributed to CAD may be totally disabled and yet have entirely normal coronary arteries!*

The status of the collateral circulation is presently controversial, but collaterals appear to signify severe CAD (117).

Several reports have appeared of patients, particularly young females, with anginal-type pain, and sometimes with an abnormal resting or exertional ECG and lactate production, who have normal coronary arteriograms. This has been noted in as high as 10 percent of cases in one referral center (118). The prognosis of these patients has appeared to be good in general, although rarely patients have subsequently died, demonstrating single or multiple subendocardial infarctions. The status and etiology of this problem are presently unknown. Cardiac hypoxia, small coronary disease, vasospastic phenomena, stagnant flow, faulty regional distribution of blood flow, altered thrombogenesis, blood viscosity and intracellular metabolism and oxidative processes, smoking and abnormalities of hemoglobin-oxygen transport and dissociation ("stingy hemoglobin") have been mentioned as etiological factors. Technically poor arteriograms and misinterpretations of the films, anxiety neurosis, neurocirculatory asthenia, vasoregulatory asthenia, chest wall pain, cardiomyopathies, neuromuscular diseases, RHD, pectus excavatum, the systolic-click syndrome, and the mimics of reflux esophagitis, gallbladder disease, cervical osteoarthritis and extrasystoles may explain some of these puzzling cases (119, 120, 121, 122).

Variant AP of Prinzmetal has been generally presumed to be due to a significant focal obstruction in a major coronary artery and thus ideal for a bypass graft. However, Cheng and co-workers recently reported 5 cases, 4 of whom had normal coronary arteries, and identical electrocardiographic changes in the presence or absence of pain (123, 124).

Some patients have had a clinical diagnosis of a MI (with ECG and enzymes) in whom no obstructive disease was seen on coronary arteriograms. Campeau summarized possible explanatory factors: the lysis of

coronary emboli (125) and recanalization of thrombi, a pulmonary embolus, myocarditis or pericarditis; an overlooked occlusion, a temporary occlusion by spasm and changes in the microcirculation, abnormal blood clotting or platelet conglutination; or the infarction may not have been caused by a coronary occlusion, in that other previously mentioned factors, decreased coronary blood, precapillary A-V shunts, congenital anomalies of the coronary arteries, hypertrophic cardiomyopathy, nonischemic necrosis (carbon monoxide, contusion, cardiac vein thrombosis) or acute pancreatitis were the important factors (120). Other possible causative factors have been cited recently, such as estrogen therapy, fibrosis of the myocardium without CAD, luteal ostial occlusion, periarteritis nodosa, myocardial bridging and dissecting aneurysm of the aorta (126, 127). It is the opinion of some authorities, however, that small vessel disease causing myocardial ischemia (too small to be demonstrated on Sones-quality arteriograms) is less than 1 in a 1000 cases, if it exists at all (128).

Prognosis

Prognosis is poor if obstructive disease has caused LV dysfunction. The 5-year survival is reduced for patients with multivessel obstruction (48 percent) but is 95 percent for patients with mild or moderate disease. The Cleveland Clinic experience revealed that 62 percent of patients with triple-vessel disease, but only 15 percent of those with single-vessel disease, were dead at the end of 5 years (108). (4 percent yearly attrition rate for AD and 1.8 percent for RCA or circumflex disease; about 6 percent yearly for 2-vessel disease). This group recently found that the coronary arteriogram contains major predictive information. In patients with normal arteriograms the prognosis was excellent (observed mortality < expected rate), while patients with slight vessel-wall irregularities had a favorable prognosis (mortality rate same or < expected; for patients with moderate abnormalities (30 to < 50 percent narrowing), the prognosis is greater than expected, and represents the early phase of progressive coronary atherosclerosis. Life threatening disease is not frequently overlooked by arteriographic methods, and future death correlates well with the degree of coronary disease (129).

High-grade stenosis of the main left coronary trunk has a very poor prognosis, requiring urgent surgery in spite of the high operative mortality (77). There is a high risk of SD and death with CA. Left main coronary disease is associated with extensive obstructive disease

of other arteries, and may be predicted by certain clinical and laboratory findings.

CA provides information about the anatomy of the coronary arterial circulation but does not directly quantitate heart disease, cardiac function or coronary blood flow, nor does it directly disclose myocardial ischemia. It does not verify that the patients complaints are related to the demonstrated angiographic abnormalities (36, 44, 108, 130).

Objectives and Value

The objectives and additional assets of CA have been delineated by Sheldon and Sones (49, 34). It should provide a highly accurate morphologic assessment of the coronary arteries with a minimum of risk or discomfort for the patient; it should determine accurately the location of any obstruction, the length, severity, and its effect on cardiac function in the major, secondary and tertiary vessels; it should distinguish minimal, nonocclusive lumen irregularities and identify the origin and distribution of collateral vessels of 100-200 microns; total and regional LV functional characteristics (contraction, scar), and any associated valvular or other heart disease should be recognized; the morbidity and risks should be similar to most other experienced laboratories with these techniques (49).

CA serves as an objective basic standard of diagnosis. It excludes CAD as a cause for chest pain, arrhythmias and electrocardiographic abnormalities; and it is invaluable in the management of patients in respect to diet, drugs or surgical therapy, and for prognosis in young men. It serves as a basis for development of surgical techniques (34).

The most important limiting factor to broad utilization of CA has been stated to be the lack of an adequate number of well-trained physicians to perform and interpret the studies (34). The unavailability of adequate equipment is another limiting factor. The high level of required technical competence appears to require at least 2 years of special training to provide a cardiologist or radiologist with sufficient experience to perform such studies independently (34), notwithstanding the enthusiasm exhibited by certain untrained individuals.

Guidelines for the performance of CA and coronary revascularization surgery have been proposed (90, 91). A minimum for each arteriographer is 5 cases weekly, to maintain competence in performance and interpretation of the study and to minimize risks. It may require from 14-18 arteriograms per week (including postoperative studies) for a financial break-even point for many

laboratories, and to support an adequate surgical program of 3-4 surgical candidates per week.

Summary

"More than any other development, selective cine-coronary angiography is responsible for most of the exciting advances in our knowledge and management of angina pectoris" (9). The credit for this momentous contribution belongs in large measure to Dr. Mason Sones (30).

Selective coronary arteriography provides the only means for visualizing the coronary arteries in the living subject and has been found to be a highly accurate method of evaluating the morphology of the coronary vessels (103). Its reception, safety and great value as a milestone in cardiology rests upon faultless specialized catheterization, radiological and photographic equipment and processing techniques, employed by well trained technical and medical professional personnel (34, 90, 91). Its future appears bright, but is linked in part with future developments in coronary revascularization surgery. It is only indicated when a specific benefit to the patient is likely. It is indicated "when a problem is encountered which may be resolved by objective demonstration of the coronary artery tree, provided competent personnel and adequate facilities are available and the potential risks are acceptable to the patient and his physician" (13).

Resumen

"Más que ningún otro avance en tecnología de diagnóstico, la angiografía coronaria selectiva es responsable por los adelantos recientes en nuestros conocimientos y manejo del *angor pectoris*" (9). La mayor parte del crédito por esta gran contribución pertenece indudablemente al Dr. F. Mason Sones (30).

La arteriografía coronaria selectiva provee el único medio eficaz para visualizar las arterias coronarias en el sujeto vivo y ha demostrado ser un método muy preciso para estudiar la morfología de dichos vasos (103). Su aceptación, seguridad y gran valor como un puntal en la cardiología moderna depende de un cateterismo muy preciso, equipo radiológico y fotográfico de la más alta calidad, y utilizado por personal profesional, médico y técnico, muy bien entrenado (34, 90, 91). Su futuro parece brillante pero está relacionado en parte con el desarrollo futuro de la cirugía de las arterias coronarias. El procedimiento está indicado solamente cuando se puede anticipar beneficio específico para el paciente.

Podemos resumir aún más diciendo que la arteriografía coronaria selectiva está indicada "cuando se encuentra un problema que puede resolverse demostrando la morfología del árbol coronario, siempre y cuando se cuente con personal competente, existan facilidades adecuadas, y el riesgo potencial sea aceptable para el paciente y su médico" (13).

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EVALUATION OF PROFESSIONAL ACTUATION OF PHYSICIANS AND SURGEONS IN THE CASE LAW OF PUERTO RICO

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In the present discussion of the evaluation of professional actuation of physicians and surgeons in the case law of Puerto Rico, a word or two is necessary as to the scope of the discussion, both as to subject matter and as to the time interval covered. I am including one case in which a dentist is involved, but the issue is essentially one which could have involved a medical man or surgeon, so that the legal doctrine is highly relevant. Timewise I am including *Rojas v. Maldonado*, a 1948 case which is in Vol. 68 of D. P. R., but no cases in volumes earlier than 68. At the other end, I am including cases in Vol. 99 which enters 1971. This covers a span about twenty-three years and thirty-two volumes. With the rapid development of the law there is not much need to go farther back; and Vol. 99 is the most recently published at the time of preparation of this work.

The material to be covered is quite ample. Indeed, it extends beyond the scope of malpractice in the narrow sense — if one considers that malpractice has to do with treatment injudiciously chosen or negligently applied. To this category of cases of alleged malpractice in the narrow sense I shall address myself in the third subdivision of the paper. There are, however, other hazards which threaten the physician and these I will consider first. Accordingly, I will divide the case material into 3 groups: (1) detention of patients: 1 case; (2) operative consents: 3 cases; and (3) a number of cases of treatment in the narrow sense.

Issues in legal actions are seldom uncomplicated, and the final resolution of the court does not always depend on the aspect of the case most interesting to the doctor. Sometimes technical, accidental or contingent matters serve as the basis for the decision so that the actuation of the professional man is never precisely evaluated.

Such is the case in *Dobbins v. Hato Rey Psychiatric Hospital*, 87 D. P. R. 30, 1962. Despite the abbreviated designation of the case, the original suit was against the Commonwealth of Puerto Rico, the Hato Rey Psychiatric Hospital, and the doctor, who working for the State Insurance Fund, was therefore an employee of the Commonwealth of Puerto Rico.

The facts as set forth are to the effect that the doctor, working for the State Insurance Fund, sent the patient with a sealed letter directing her hospitalization to the Hato Rey Psychiatric Hospital. She was not apprised of the content of the letter; she was merely told that she was being sent to the hospital to be interviewed by a psychiatrist. Once there, however, she was detained from Wednesday 16 March until Sunday 20 March 1960. Subsequently she filed suit for damages against the Commonwealth, the Hospital and the doctor. The suit against the Commonwealth was dismissed and the plaintiff appealed.

The case was finally decided on essentially legal grounds. The confinement of the patient originated in the order of the doctor, an employee of the Commonwealth. The order of hospitalization is the basis for the suit. By virtue of a doctrine known as sovereign immunity, the Commonwealth is, in general, immune to claims. However, the Commonwealth in a special law has waived its immunity for certain acts of its employees, but these acts do not include illegal detention which is at issue here. So the lower court was correct in dismissing the claim against the Commonwealth. Moreover, by provision of the same law, a judgment in an action against the Commonwealth precludes action against the employee. So the Supreme Court does not have to evaluate the professional conduct of the physician in ordering the detention. The Court does make mention of the law governing commitment to mental institutions, so there is at least a hint of impropriety in the physician's behavior.

We now proceed to the cases in which the matter of consent for operation plays a prominent role. The earliest of these in our series is *Rojas v. Maldonado*, 68 D. P. R. 818, 1948, a most tragic case. The facts

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are as given credence by the Supreme Court. A four-and-a-half-year old child was admitted to the defendant's institution to be operated on by a certain surgeon; but the defendant operated on the patient without consent. The child died as the result of the operation. The parents sued for damages, basing their claim on (1) operation without consent and (2) lack of care and skill on the part of the operating surgeon. The lower court awarded damages on the first claim, that of operation without consent, but as to the second cause of action, negligence and lack of skill, found the evidence insufficient to support the claim. Both parties appealed. The plaintiffs were dissatisfied with the amount of the award and complained about the dismissal of the claim based on negligence. The defendant appealed on the grounds that it was not proved that the child's death resulted from the defendant's fault or negligence.

The Supreme Court of Puerto Rico decided against the defendant in this regard, holding that when an operation is carried out without consent, under circumstances that do not constitute an emergency, lack of consent by itself is sufficient to render the surgeon responsible for untoward results. No showing of negligence or of lack of skill or expertise in the procedure is necessary to establish his responsibility. The legally effective causal nexus goes directly from the lack of consent to the harm — in this case the child's death. Negligence or lack of skill in execution is not a necessary intermediating factor. It should be pointed out here — and I cannot stress it too strongly — that what constitutes cause in the legal sense is in itself a matter of law. Legal cause is what a judge says it is. Whatever causation is in the scientific or medical sense — and the matter plunges one immediately into metaphysics — in the legal sense it is comparatively simple. The judge — or sometimes the legislator — defines it. In this case, then, the Court defines the cause of the harm as the illicit act consisting in operating in the face of lack of consent.

The Supreme Court points out, in the case we are discussing, that if a surgeon operates with due consent, he is responsible for untoward results only if negligence or lack of skill mediate; but when a surgeon operates without consent, he commits an illicit act and no negligence or lack of skill need be demonstrated to establish his liability in the event of harm. As to negligence or lack of skill on the part of the defendant, these had not been convincingly demonstrated, therefore he is not held to be liable on that score.

The companion case to *Rojas v. Maldonado* is *Montes v. Fondo del Seguro del Estado*, 87 D. P. R. 199, 1963. From a legal standpoint the case hinges on the question

of the liability of the Commonwealth, as does *Dobbins*, through the State Insurance Fund. The suit in *Montes* is not against the surgeon; but it is his actuation that is the basis for the suit, on the grounds that he operated without due consent. In this case, the surgeon examined the worker-patient for the State Insurance Fund and recommended operation for multiple nucleus pulposus herniation. The worker, who had been hospitalized for studies, went home while the Fund decided whether he should be operated upon. The Fund did, indeed, so decide, and ordered his re-hospitalization.

He was operated upon and three lumbar discs were removed. However, he suffered a paraplegia. The Fund determined that he was completely and permanently incapacitated and conceded him the maximum allowable. However, he sued the Fund and the Commonwealth, alleging that the operation was carried out without his knowledge or consent, and, moreover, that it was carried out negligently. In regard to this last, no evidence was presented that showed negligence.

The lower court first decided that the Commonwealth was liable because the Fund had ordered the operation without the consent of the plaintiff. Upon reconsideration, however, the lower court reversed itself.

The lower court's final reasoning was as follows. Operation without consent is technically a battery or aggression against the person. Battery stands on the same footing as illegal arrest or detention, which we have already discussed, in the law concerning suits against the Commonwealth for acts of its employees. The Commonwealth does not waive its immunity when its employees are guilty of either of these offenses against the person. Accordingly, the lower court, in its reconsideration, dismissed the suit against the Commonwealth.

The Supreme Court reversed the decision. True, operation without consent is battery, but only technical battery. The intention to commit a wrongful act is not present. The law in question refers to malicious and wilful acts. So the merely technical battery committed by the operating surgeon is not that battery to which the law refers. Accordingly the Commonwealth is liable after all.

The interpretation of the law governing Commonwealth liability need not concern us. What does concern us is the evaluation that the Supreme Court makes of the actuation of the surgeon. By operating without consent he committed a battery, albeit a technical battery.

If we may be permitted a comment, we would sug-

gest that the surgeon might very well assume that the worker-patient had implicitly, by re-entering the hospital, consented to the operation. Certainly the operation was the apparent purpose of his readmission, although he was later to allege unawareness. The intermediary role of the Fund, moreover, may have helped to entrap the surgeon into thinking he had proper authorization to operate. In *Rojas* the surgeon, the lower court found, had confused the application for hospitalization with an operative consent. In both of these cases there were, it would seem, extenuating circumstances.

We have one more case which touches upon the matter of operative consent. In *Torres Pérez v. Hospital Dr. Susoni, Inc.*, 95 D. P. R. 867, 1968, the patient's leg was amputated for gas gangrene and the patient later sued for negligent and inadequate treatment. His complaint was dismissed. He appealed and cited as error of the lower court the latter's failure to find that he was operated upon without his consent, using as precedent *Rojas v. Maldonado* and *Montes v. Fondo del Seguro del Estado*. However, in this case, his sister, who had assumed responsibility, had given consent. The patient was in danger of dying if the amputation were not carried out in time; moreover, apprising him of the necessity in advance could have been expected to produce such untoward psychological effects that it was not feasible to do so. Accordingly the Supreme Court confirmed the lower court's decision in dismissing the case.

We now reach the cases where the treatment as such, and the manner of applying it, come into question. A most fascinating case from a medical standpoint is *Rivera v. Dunscombe*, 73 D. P. R. 819, 1952, in point of time the first of this series.

In this case the physician gave the patient a caudal injection for pain of the sciatic type in February 1948. The patient shortly after developed a lumbar abscess. However, the patient had previously, in December 1947, i.e., before the caudal injection, been treated for an affection that was diagnosed as lumbago; his disorder was located in the girdle region, toward the back. He was treated with penicillin at the time. One of the principal issues of the case is whether the "lumbago" of December represented the abscess of February, or whether the intervening caudal injection, through improper asepsis, had introduced the causative organism — colon bacillus — of the abscess. The plaintiff claimed the physician defendant had failed to sterilize the area of the injection, an allegation disputed by the physician and his assistant, and apparently not credited by the lower court.

The lower court dismissed the plaintiff's claim. In the course of the decision the court enunciated the principle that no presumption of negligence arises from the (mere) fact that the patient should have suffered harm. In confirming the action of the lower court, the Supreme Court summarizes the principles that operate in this and similar cases. A physician is only obliged to give to his patient such attention as is generally employed for similar cases by the other physicians in the community. He is liable for damages only when he has acted negligently, with carelessness or lack of skill. The presumption exists in favor of the physician that he selected and applied the proper treatment to his patient, no presumption of negligence arising from the fact that the patient should have suffered harm or that the treatment should not have been successful. Neither does any inference or presumption of negligence arise from the fact of an infection's having developed after an operation or other treatment. The physician's negligence, *per se*, is not sufficient to recover damages. Once established the fact that the physician has been negligent, it is necessary to establish that this negligence was the proximate cause of the injury received. The mere possibility that the negligence of a physician should have been the proximate cause of the injury is not sufficient to establish a case of malpractice. If the possibility exists that other causes may have intervened, it is the obligation of the plaintiff to exclude them and to show that the negligence of the physician was really the proximate cause of the injury.

In *Sáez v. Municipio de Ponce*, 84 D. P. R. 535, 1962, an 11-year-old little girl had a sore throat, headache, and cough. She was examined by an interne in a hospital operated by the city of Ponce. The doctor found that her tonsils were inflamed, and she had rhonchi in the chest. In the presence of her grandmother, who accompanied her, the child was asked whether she had been given penicillin by injection previously, and what her reaction had been; she replied that she had been given injections of penicillin, but had never had an allergic reaction to it. She was not tested further in regard to penicillin sensitivity. Nevertheless, given an injection of penicillin by order of the interne, in a matter of minutes she collapsed and died. The city of Ponce was sued. The lower court decided against the plaintiff, who appealed.

The plaintiff based his appeal in large part on the fact that the interne was not licensed, but this, the Supreme Court ruled, does not constitute foundation for an action in damages for negligence or lack of skill in the absence of a demonstration of causal relationship

between the injury and the lack of a license.

As for recognition of the anaphylactic condition of the patient, the lower court determined that the prevalent practice in the community had been observed: this was limited to inquiry as to the patient's past reactions with the drug. It was not even insinuated that the administration of penicillin was not the indicated treatment.

The Supreme Court, moreover, cites *Rivera v. Dunscombe* and says that the plaintiff must establish by the preponderance of the evidence — credited by the trier of the facts — that the injury was caused by negligence or inexpertness of the physician. The presumption exists, in absence of evidence to the contrary, that a reasonable degree of care has been exercised and the proper treatment given. The plaintiff has to present sufficient evidence to controvert this presumption; this evidence must show more than the mere possibility that the injury was due to the physician's dereliction. The Supreme Court, in *Sáez*, confirms the lower court in dismissing the complaint.

Guzmán v. Silén, 86 D. P. R. 532, 1962, equates the care and skill required of dentists to those of physicians and surgeons. In this case a dentist was sued. He had extracted a left first molar and an antro-oral fistula developed. The dentist continued treating the patient with additional operations, but matters went from bad to worse, the dentist carrying out six operations in all. The patient suffered pain, loss of weight, and sleeplessness. He consulted a physician and as a result reached a dental surgeon who was able, in a matter of weeks, to restore him to an almost normal condition. More than three months had elapsed, however, between the first operative procedure by the defendant and the time that the patient reached the dental surgeon.

The lower court concluded that the practice in the community was for the dentists in general practice to refer cases with antro-oral fistulas to oral surgeons. The lower court accordingly awarded damages to the plaintiff and the defendant dentist appealed. The Supreme Court confirmed: the lower court did not err when it found the defendant negligent in failing to refer the patient to a specialist.

In *Pérez v. Municipio de Mayagüez*, 87 D. P. R. 620, 1963, no physician was involved but we mention the case briefly. A child died of anaphylactic shock after an antitetanic injection. She had been tested for sensitivity with negative results. In this case the suit was against the hospital; the injection was given by a nurse following the routine practice in the hospital. The lower court

dismissed the claim and the Supreme Court confirmed.

Castro v. Municipio de Guánica, 87 D. P. R. 725, 1963, also has to do with an injection by a nurse, this time of phenobarbital sodium. The patient was later found to have a sciatic nerve lesion. The examining neurosurgeon, however, could not state definitely that the lesion had been caused by a needle. The lower court found liability, but the Supreme Court, on the basis of the lower court's mistaken application of the doctrine of *res ipsa loquitur*, reversed.

Ramos Orengo v. La Capital, 88 D. P. R. 315, 1963, based its action in part on the fact that a patient who had a sudden, unanticipated convulsive seizure was permitted to fall from a stretcher; since this attack could not have reasonably been foreseen, there is no liability for negligence. The other base for the action had to do with the treatment the patient received after the fall; he was five days in the Municipal Hospital with a fractured and discolored knee. He was to be operated upon on the sixth day. However, he was instead transferred to another hospital where he was operated upon. The plaintiff failed to present evidence to refute the presumption that exists in these cases that the treatment administered was correct. Yet the lower court found liability. The Supreme Court reversed: it requires expert testimony to refute the presumption of correct treatment. Here, however there is no demonstration that the five days wait in the hospital constituted negligence. As in *Sáez*, the presumption of correct treatment exists. It is the burden of the plaintiff to refute this presumption.

Amaral Amaral v. Fortuño, 93 D. P. R. 834, 1966, takes us away from the question of proper treatment as such. The doctor's liability here, according to the Supreme Court, arose from permitting a visually impaired patient to fall while attempting to leave an examining table. The patient, recently operated on for retinal detachment, suffered greatly impaired prospects for visual restoration as a result of the fall. The doctor was aware of the patient's recent eye operation and should have assisted him from the table. In not doing so, the doctor failed to exercise due care.

Pérez v. E. L. A., 95 D. P. R. 745, 1968, is a heartrending case. On 14 August 1961 the mother of a thirteen-month-old little girl found her on the kitchen floor with symptoms of suffocation. Some beans were scattered about. The baby was taken to the Health Center at Ciales where the doctor examined her and observed that she had symptoms of suffocation as if by a foreign body. He accordingly referred her to the Arcibo District Hospital where there were more facilities

for treating such cases. In his referral note the doctor mentioned that the child had nausea and that she coughed as if trying to vomit. He recommended examination for a foreign body in the esophagus.

At the Arecibo District Hospital the child was seen by the doctor there, who wrote, "The mother claims that the child swallowed a pin." The doctor ordered X-rays. These were reported, "Negative for foreign body." The child was sent home. The mother testified that the child was smothering and trying to vomit. During the night she became black and without breath. The mother took her to a private practitioner, who sent them back to the Arecibo District Hospital, giving the mother a note to take along with his impression of a foreign body. The mother testified that she arrived at the Hospital about 1:15 a.m. 15 August. The child was seen by a different physician from the one who had previously seen her. He made the provisional diagnosis of "foreign body." As to treatment he wrote, "X-rays negative. Sent home." The child continued with her symptoms. 17 August she was taken to another private practitioner, who prescribed medicine. She continued ill. She died 22 August. The autopsy showed a bean at the tracheal bifurcation.

The parents sued the Commonwealth. The lower court failed to find negligence. The plaintiffs appealed, pointing out as error the lower court's having exonerated the two doctors at the Arecibo District Hospital of negligence or lack of skill which caused the death of the child. The Supreme Court reversed. As a medical witness — the doctor of the Health Center at Ciales — testified, the pharynx should have been examined down to the trachea. The legal cause of the death was negligence or negligence and lack of skill on the part of the doctors.

We have already discussed the case of *Torres Pérez v. Hospital Dr. Susoni, Inc.*, 95 D. P. R. 867, 1968, in regard to the question of the operative consent. However, the plaintiff also sued for damages on the alleged grounds of negligence and improper treatment. He had been involved in an automobile accident. The road was wet and he lost control of the car he was driving, which left the road and struck a tree. He suffered dislocation of the right knee and an open wound about 5 to 6 inches long and somewhat over an inch deep in the right popliteal region in which particles of earth were found. The wound was cleaned and debrided, then sutured and the dislocation reduced. A circular cast was applied. He was also given treatment to prevent tetanus, gas gangrene, and other infection. The patient was seen by a doctor at least twice a day. He nevertheless developed

gas gangrene and, as we have seen, his leg had to be amputated. He sued, trying to relate the gangrene to pressure by the cast or to infection acquired in the hospital. During the trial the difference between gas gangrene and pressure gangrene was explained by medical witnesses. The measures which the defendant hospital used to prevent the spread of infection were also attested to. The lower court dismissed the claim, and the Supreme Court confirmed.

In *Cabrera v. Asoc. de Señoras Damas*, 96 D. P. R. 775, 1968, a doctor prescribed Furacin Ophthalmic Solution for an infection of the eye, but the hospital employees administered Furacin Otic Solution. The patient's husband, a pharmacist, alerted by the patient's complaints of burning, became aware of the error. The patient finally lost the eye, which had to be enucleated; this might have been necessary even without the erroneous application. Both the doctor and the hospital were sued. The lower court dismissed the suit. On appeal, the Supreme Court confirmed the dismissal in regard to the physician who, according to the evidence, acted diligently, but found the hospital liable for damages.

In *Vda. de Torres v. Womble*, 99 D. P. R. 859, 1971, the claim is based on a vesico-vaginal fistula that developed some days after abdominal hysterectomy for cervical carcinoma *in situ* complicated by ovarian cysts and adhesions; the right ovary and tube were removed as well as the uterus. The lower court did not find evidence of negligence and dismissed the claim, concluding that vesico-vaginal fistula is a complication of the operation that does not necessarily show negligence on the doctor's part.

In this case the Supreme Court, confirming the action of the lower court, reviews the relevant doctrine. It mentions *Sáez and Rivera v. Dunscombe*, which we have discussed. It recalls, from *Ramos Orengo*, the presumption of reasonable care and proper treatment, which the plaintiff, in order to establish a claim, must controvert by means of evidence to the effect that there is something more than a mere possibility that harm to the plaintiff is due to fault of the doctor. The Supreme Court also recalls from *Guzmán v. Silén* the need to establish proper professional practice by means of expert testimony. In *Pérez v. E. L. A.* the presumption of due care was refuted; the professional practice in the community as a norm does not mean poor practice, but the practice that meets recognized professional standards.

The Supreme Court then goes on to discuss the doctrine of *res ipsa loquitur*, which it decides does not

apply to this case. Accordingly — although it has not been decisive in deciding any of the cases we have considered — we will discuss this doctrine briefly here.

The original case that established the doctrine of *res ipsa loquitur*, was one in which a barrel of flour fell out of the window of a warehouse and injured a passer-by. The mere layman *presumes* that people should not permit barrels to fly out of windows: in such a case, on the face of the matter, the layman *presumes* negligence, without any need for seeing what happened inside the warehouse or requesting the opinion of an expert on warehouses. This presumption, let us hasten to add, is rebuttable by the defendant but if the defendant does nothing, the presumption stands. The presumption is given more weight in some jurisdictions than in others; in Puerto Rico it is reduced to an inference.

The doctrine of *res ipsa loquitur* obviated the need for expert testimony in such malpractice cases as finding a pair of scissors left in the abdomen of a patient. The barrel and the scissors were solid enough, but not all applications of the doctrine have been equally so. Indeed, it became so expanded that it degenerated almost to a matter of *petitio principii*, begging the question, and assuming the negligence that the plaintiff hitherto had to prove.

In *Vda. de Torres* the mere occurrence of the vesico-vaginal fistula does not establish the presumption of negligence. Expert testimony in this case cited an incidence of 10 percent in cases of hysterectomy. It is a risk inherent in the operation. It can occur even when the operation is performed carefully and in accordance with proper practice. Therefore the inference of negligence is not permissible.

In *Rivera v. E. L. A.*, 99 D. P. R. 890, 1971, a patient with a long history of urinary calculi entered the hospital 30 October. His admission diagnosis was of renal lithiasis and chronic pyelonephritis. He did not do well and was operated on 5 November at which time acute peritonitis, possibly but not certainly from a perforated appendix, was evident. He died the next day. The survivors sued. The lower court awarded damages, inferring negligence, and citing *Pérez v. E.L.A.*

The Supreme Court reversed. The presumption

of correct treatment and reasonable care exists in the absence of evidence to the contrary. If the doctor exercises care in the diagnosis according to community practice he is not liable even if the diagnosis constitutes error of judgment. He ought to have latitude in the exercise of reasonable judgment. Responsibility does not arise for error in the diagnosis of obscure symptoms. The testimony of other physicians that they would have made a different diagnosis or disagreement among them as to the diagnosis does not in itself justify the conclusion of negligence.

In the present case there was no evidence that the doctors did not act within the community norms in examining and caring for the deceased. The symptoms were confusing in spite of attention and multiple examinations. This case is different from *Pérez v. E. L. A.* in which, despite the diagnosis of foreign body, the child was sent home because the X-ray examination was negative.

This has been an exceedingly rapid and cursory survey of some extremely interesting case law. It can hardly be summarized further. While each of us fervently hopes he will never have need to apply it in retrospect, perhaps foreknowledge may be of some utility.

Cases

- (1) *Dobbins v. Hato Rey Psychiatric Hospital*, 87 D. P. R. 30, 1962.
- (2) *Rojas v. Maldonado*, 68 D. P. R. 818, 1948.
- (3) *Montes v. Fondo del Seguro del Estado*, 87 D. P. R. 199, 1963.
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- (5) *Rivera v. Dunscombe*, 73 D. P. R. 819, 1952.
- (6) *Sáez v. Municipio de Ponce*, 84 D. P. R. 535, 1962.
- (7) *Guzmán v. Silén*, 86 D. P. R. 532, 1962.
- (8) *Pérez v. Municipio de Mayagüez*, 87 D. P. R. 620, 1963.
- (9) *Castro v. Municipio de Guánica*, 87 D. P. R. 725, 1963.
- (10) *Ramos Orengo v. La Capital*, 88 D. P. R. 315, 1963.
- (11) *Amaral Amaral v. Fortuño*, 93 D. P. R. 834, 1966.
- (12) *Pérez v. E. L. A.*, 95 D. P. R. 745, 1968.
- (13) *Cabrera v. Asoc. de Señoras Damas*, 96 D. P. R. 775, 1968.
- (14) *Vda. de Torres v. Womble*, 99 D. P. R. 859, 1971.
- (15) *Rivera v. E. L. A.*, 99 D. P. R. 890, 1971.

CARTA AL EDITOR

Dr. Jorge O. Just Viera, Editor
Boletín Asociación Médica de Puerto Rico
Santurce, Puerto Rico

Estimado doctor Just:

Deseo por este medio felicitar al doctor José E. Sifontes, editor invitado, por su acertado editorial sobre las indicaciones para la amigdalectomía, Boletín Asociación Médica de Puerto Rico, volumen Núm. 65 Núm. 4.

La incidencia de amigdalectomías en los hospitales públicos y privados de Puerto Rico es alarmante. Difiero de la opinión del doctor Sifontes de que la morbilidad y mortalidad en nuestros hospitales es desconocida ya que en nuestra experiencia el sangramiento post operatorio, aún dos a tres semanas después de la operación, es observado con bastante frecuencia haciendo necesario en muchos de estos casos la readmisión al hospital.

No puedo dejar de recordar el resumen que hacía el doctor Francisco L. Raffucci de las indicaciones para amigdalectomía: "The only indication for tonsilectomy is obstruction of the airway".

Sinceramente,

José J. Cerra Díaz, MD
Jefe de Cirugía
Hospital Subregional Caguas

EL RECORD POR PROBLEMAS

Todos estamos conscientes de que en la sociedad contemporánea existe un intenso interés por que se mejore la efectividad de los servicios médicos. Sin entrar en las razones o las sinrazones de los muchos aspectos que tiene ese interés, podemos dar por sentado que un elemento esencial y fundamental del problema es el expediente médico.

Cada contacto, cada información, cada evaluación y cada acción que resulta del encuentro médico-paciente queda documentada únicamente en el expediente médico. Por lo tanto, cualquier deficiencia en esa fuente de información resulta en disminución de la efectividad diagnóstica y terapéutica, del aprovechamiento que podemos recibir de la experiencia, y de la confiabilidad de los datos que puedan ser usados como base para el análisis de la efectividad del servicio.

La literatura médica ha estado documentando el descontento general que existe con el expediente médico según lo preparamos al presente. Se ha concluido que el método tradicional resulta en un expediente incompleto, que da insuficiente información, y que es torpe como instrumento de enseñanza.

Una posible solución que promete mejorar significativamente el sistema actual es el "Problem Oriented Record" preconizado por Lawrence Weed y que nosotros hemos traducido al vernáculo como el "Record por Problemas". Ciertamente no ha sido aceptado universalmente, y bien puede ser que no sea la solución final, pero no obstante, se puede advertir la tendencia hacia este sistema por la cantidad de literatura que se está generando sobre él, por la actitud de la Comisión Conjunta sobre Acreditación de Hospitales y por las recomendaciones de las Juntas de Especialidades. Además, es digno de notar el que los programas precursores de las organizaciones de evaluación profesional (PSRO) y los anteproyectos de Seguro de Salud Universal están incluyendo en su programación este sistema o uno parecido.

Dejando a un lado por el momento las ventajas que en términos de mejor diagnóstico, mejor tratamiento, mejor educación y mejor investigación el "Record por Problemas" pueda ofrecer, queda el hecho de que a los ojos de los planificadores de salud en todo el mundo, la organización sistemática del expediente médico es necesaria para evaluar propiamente la calidad del servicio y la efectividad del uso. Además se considera que es la única forma en que puede obtenerse información utilizable para poder mejorar la efectividad del servicio mediante un proceso de retroalimentación.

La marcha hacia la ejecución de estas metas parece inexorable en este momento. Las otras ventajas del "Record por Problemas" prometen ser numerosas y deseables. Recomendamos por lo tanto, el que se establezcan como objetivos de educación personal el informarse sobre el "Record por Problemas", el aprenderlo a usar, y el empezar a implementarlo en la práctica diaria. Invitamos la asistencia de todos los médicos a la discusión a panel que sobre este tema se llevará a efecto durante el curso de la convención de la Asociación Médica de Puerto Rico este año.

Elí A. Ramírez-Rodríguez, MD, MS, FACP

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VOCATIONAL REHABILITATION AND THE INJURED WORKER

Legend has it, before making Earth, God drew a picture and showed it to the angels. They were so overwhelmed that they requested permission to caucus. After several days, they were granted an audience to express their collective opinion. They told God that Earth would be superior to Heaven and so beautiful that even the angels would want to live there. This, they said, was unthinkable, because there should be only one Paradise in the Universe, and it should be God's Heaven. Unfortunately, the angels caucused too long, and God had created Earth already. However, He was so impressed with their argument that He decided to spoil His creation. This is why He placed Man on Earth.

Now, whatever this story of Man's spoiling Earth has to do with "Vocational Rehabilitation and the Injured Worker" can be ascertained simply by reviewing the Workmen's Compensation Laws of the Fifty States, the Commonwealth of Puerto Rico and the Territories of the Union. Although they all talk about the same thing, each one is different. What's more, the interpretation of these statutes varies not only from region to region but from referee to referee in the same area.

An analysis of the benefits found in most Workmen's Compensation Laws excludes vocational retraining from the overall treatment of the disabled worker despite the fact that rehabilitation is considered an integral part of complete medical care today. However, most States have special provisions which throw this burden on their Divisions of Vocational Rehabilitation, expanded by the Federal Vocational Rehabilitation Act of 1954.

How effective these programs are for the injured worker can be determined only by impartial studies in each locale. Those that have been reported emphasize invariably the need to contact the patient early in his convalescence in order to direct his thinking towards vocational readjustment. The motivation for retraining must be established long before the maximum medical benefits have been reached. If you wait until the economic advantages of disability have become firmly ingrained in the patient's mind, the resulting neuroses will bury most assuredly any remaining ability. Then, you can truly paraphrase "The flesh is willing, but the spirit is weak"!

The special provisions that each jurisdiction has in their Workmen's Compensation Laws to cover vocational rehabilitation are based on sound judgement. Unfortunately, very few take into consideration the psychological necessity of sending the vocational counselor early. Only one State, Minnesota, specifically advocates, "The Division of Vocational Rehabilitation shall evaluate employees suffering more than 26 weeks disability for retraining". Minnesota also grants a maintenance allowance in the form of an additional compensation of two-thirds of the daily wage for a maximum of 104 weeks. Many of the States, believe it or not, still have no requirement by law for rehabilitation of disabled workers.

All of us should learn from the example of our neighbor from the North, Canada, who was certainly the innovator developing centers for the rehabilitation of injured workers in this hemisphere. The Canadians understood long ago the need to provide the means whereby their handicapped workmen could reach their maximum physical, emotional, social and vocational potentials. Canada not only was the pioneer but has consistently maintained leadership in this program. Today, the Province of Ontario sets "no limit on amount in any one case or in any year for rehabilitation".

If this procedure is morally and economically sound for Ontario, why should it be less so for the States of the "Greatest Nation on Earth".

This is precisely why I chose the Ontario Workmen's Compensation Rehabilitation Center on East Richmond Street under Dr. Harold Storms to start my training in physical medicine and rehabilitation over a quarter of a century ago. He was a poor man with rich thoughts. Many considered him a curmudgeon, and he was certainly rough on me. Under his tutelage, however, I learned that no one was totally disabled despite his physical handicap if he was mentally alert. There was always some gainful task for him in his community. A job, however menial, still carried with it the dignity of being once again a paying member of the human race. Subsequently, I followed Dr. Storms to that really great rehabilitation center at Malton. This program was administered by Mr. Ian Campbell, who taught me the wisdom of having the social worker and the vocational counselor visit the severely disabled worker early in his recovery period.

Everybody agrees that peace of mind is one of the greatest assets in healing a broken body. Yet, I know of very few hospitals that consider the services of a social worker and/or a vocational counselor necessary in the curative stage. Medical science has advanced to the point where a prosthesis is applied in the operating room immediately following an amputation. But, when does the vocational counselor get to see the patient to talk about his future job? Usually, weeks after final discharge and closure of his case. Believe me, the severely disabled worker would fare much better, if the vocational counselor brought him his first compensation check.

My thesis today is not to repeat that rehabilitation of the injured worker is a public duty and that early rehabilitation reduces disability. This was done twenty three years ago, in 1950, at the meeting of the National Conference on Workmen's Compensation and Rehabilitation in Washington, D. C. This was the first program sponsored jointly by two agencies of the Federal Government, the Federal Security Agency and the U. S. Department of Labor, to recognize the then-existing need for improving rehabilitation services to injured workers throughout the country. In order to comprehend the advances in this field in the States, you have only to pull out the copy of the "Proceedings" of this conference from your files and review it. That Puerto Rico was recognized nationally at this time for its program of rehabilitation of injured workmen may come as a surprise to many of you, but it was true, nevertheless.

Puerto Rico appreciated from the very beginning the value of combining the services of the State Insurance Fund and the Division of Vocational Rehabilitation to retrain the disabled laborer and make a tax-paying citizen out of him. Perhaps, this arrangement is easier here because both agencies are government. In Puerto Rico, there is no third-party, no private insurance company, selling workmen's compensation coverage.

On March 29, 1968, the Governor of the Commonwealth of Puerto Rico signed Law No. 11 amending section 2 of Law No. 182, approved May 1, 1951, authorizing the State Insurance Fund to invest \$200,000 annually for the sole purpose of vocational rehabilitation of injured workers. This law permits the Manager of the State Insurance Fund, to use any part of this sum to purchase services from private sources if not available from public agencies. The law clearly stipulates that any corresponding matching funds from the Federal Government must be used for the expressed purpose of vocational rehabilitation of injured workers of the State Insurance Fund.

The opening paragraph includes the following, "This action on the part of the system of compensation for accidents resulting from work responds to a modern philosophy, realistic and of great human value. It offers the disabled worker the necessary resources to contribute to his own welfare and that of his family by facilitating the most rapid rehabilitation possible in order to return him to his job; and, therefore, his life will be useful and productive".

This, of course, is in addition to the rehabilitation center of the State Insurance Fund in the

Medical Sciences Campus of the University of Puerto Rico in Río Piedras and four smaller centers scattered throughout the Island.

Two Hundred Years ago, Edmund Burke wrote "Government is a contrivance of human wisdom to provide for human wants". Certainly, all of you will agree that the best government takes care of all the needs of its people. Will all of you confirm that you have the best Workmen's Compensation Laws? If true, then you must pay careful attention to the special provisions in your statutes for the rehabilitation of the injured worker and especially the vocational retraining benefits. Each of you must judge your particular program, because each jurisdiction insofar as workmen's compensation is concerned is legally and literally an "island within itself".

Any criticism, therefore, should not be leveled at the law, but, perhaps, at the implementation of the law. There is no one to blame for a work accident, surely not the employee and least of all the insurer. Yet, there are still many judges and referees that blame the employer every time. If these same mentors were as keen on demanding early vocational retraining for the injured worker prior to fixing his disability rating, there would be fewer neurotics and many more useful people in society.

Constructive criticism, unfortunately, is not enough to solve the admitted need for better vocational rehabilitation of the injured worker. Invariably, a compromise is reached, which totally loses sight of the original tenet. If we truly comprehend what is the greatest good for the injured worker and soar above vested interests, be they political or economical, we can once more make the worker's life useful and productive. This is certainly more logical than having him request social security benefits the day after he gets his disability settlement and remain bitter with society because he was turned down and then referred for vocational retraining.

Now, all the States have second-injury provisions by law. Why not prevent the second-injury by employing the disabled worker in a job for which he has been retrained. Putting teeth into your respective Workmen's Compensation Laws to insure early vocational rehabilitation will not bankrupt the carrier of your State Compensation Insurance Funds. On the contrary, it will save your Government large sums as well as provide a source of skilled manpower for the future.

God did not spoil this beautiful Earth by placing Man on it, because He endowed His image with the ability to reason. Today, the whole world, to borrow a phrase from Dean Acheson's magnificent autobiography, lives in each other's back yard. My purpose is to get you to really know and love your neighbors, to think, to criticize and to improve. If I can but sow in your fertile minds the advantage of contacting the injured worker early in his recovery stage to prepare him for vocational rehabilitation and to motivate him constantly towards this goal throughout his convalescence, this communication most assuredly will bear fruit.

Herman J. Flax, M. D.

NOTICIAS

NEWS RELEASE FROM AMERICAN COLLEGE OF CHEST PHYSICIANS:

CHICAGO—The rapid changes in cardiac catheterization techniques and methods of evaluation will be the theme of the first postgraduate course of the 1973-74 American College of Chest Physicians Calendar of Meetings.

The course entitled "Ventricular Function — A Practical Workshop", will be held in Santa Barbara, California, November 30 and December 1, 1973.

For registration and fee information contact: Director of Continuing Education, American College of Chest Physicians, 112 East Chestnut Street, Chicago, Illinois 60611.

COUNCIL ON ENVIRONMENTAL, OCCUPATIONAL, AND PUBLIC HEALTH - AMERICAN MEDICAL ASSOCIATION

STATEMENT ON VENEREAL DISEASES — Gonorrhea ranks first (excluding influenza) and syphilis third among the reportable diseases in the United States. During 1972, there were 767,215 gonorrhea cases reported 14.5 percent higher nationally than the previous year and more than double the number reported in 1965. Increases have occurred in all parts of the nation and in all age and sex groups, but the largest concentration of cases is in the 15-24 year age group. Allowance for both under reporting and failure to diagnose all cases as they occur suggests that the actual occurrence of gonorrhea infection last year was about 2.5 million.

The Center for Disease Control estimates that the reservoir of gonorrhea includes 6 to 800,000 females and about 100,000 males that are asymptomatic. To help reduce this reservoir of silent carriers, most states have implemented gonorrhea screening programs for females. The Center for Disease Control reports that from July 1972 to March 1973 there were 3,117,022 females screened and 158,604 (5.1 percent) had a positive test for gonorrhea. Of 664,110 females tested in private physician offices throughout the nation, 2.5 percent had a positive culture for gonorrhea. The Council urges medical societies to promote gonorrhea culture screening among females.

During 1972, syphilis morbidity (all stages) exceeded 91,000 reported cases. The number of congenital syphilis under one year of age numbered 383 in 1972. Reported cases of primary and secondary syphilis (the infectious stages) numbered 24,429, up 3 percent from the previous year, with an estimated 85,000 cases occurring annually. Because large numbers have escaped detection over the years, it is estimated that if every person in the United States could be tested for syphilis today, about 1/2 million previously untreated cases would be found.

XII INTERNATIONAL CONGRESS ON DISEASES OF THE CHEST

The interface between heart and lung disease will be the

theme of the XII International Congress on Diseases of the Chest, July 7-12, 1974 in London, England.

Further registration and fee information is available from: XII International Congress of Diseases of the Chest, c/o American College of Chest Physicians, 112 East Chestnut Street, Chicago, Illinois 60611.

FROM THE DEPARTMENT OF HEALTH, EDUCATION AND WELFARE - SOCIAL AND REHABILITATION SERVICE, WASHINGTON D. C. 20201

TO: STATE AGENCIES ADMINISTERING PUBLIC ASSISTANCE AND MEDICAL ASSISTANCE PROGRAMS

SUBJECT: President's Order for Comprehensive Freeze on Prices of Commodities and Services

On June 13, 1973, the President announced a comprehensive freeze for a maximum period of 60 days on the prices of all commodities and services offered for sale except raw agricultural products. The complete statement and applicable regulations are contained in Executive Order 11723 and the Cost of Living Council Freeze Regulations published in the Federal Register, Vol. 38, No. 115, June 15, 1973.

Each vendor shall prepare a list of freeze prices for all commodities and services which he sells and shall maintain a copy of that list available for public inspection, during normal business hours, at each place of business where such commodities or services are offered for sale. In addition, the calculations and supporting data upon which the list is based shall be maintained by the vendor at the location where the pricing decisions reflected on the list are ordinarily made and shall be made available to representatives of the Economic Stabilization Program.

"Freeze prices" means the highest price at or above which at least 10 percent of the commodities or services concerned were priced by the vendor in transactions with the class of purchaser concerned during the freeze base period, June 1-8, 1973. In computing the freeze price, a vendor may not exclude any temporary special sale, arrangement or allowance in effect during the base period. If the vendor had no transactions during that period, his freeze base period is the nearest seven-day period in which he had a transaction.

This comprehensive freeze applies to the health sector. Until modifications are adopted, all other present controls applicable to the health industry will continue.

Inquiries to: SRS Regional Commissioners

NEWS RELEASE FROM AMA:

SKIN DIVING—

Skin diving enthusiasts are gaining thousands of new recruits each summer. Thousands of Americans of all ages and sexes are spending summer weekends exploring lakes

and streams and the ocean floor from the vantage point of the fishes.

Diving makes demands on the body which are unlike those met above the surface.

Navigating under water is heavy exertion and those with respiratory problems or heart and blood vessel disease should not attempt it, says the American Medical Association. Diving is ruled out for those with perforated ear drums. Ear plugs are for surface swimming only and should not be used for diving. The depth changes also require that sinuses and ears be in good shape to equalize the pressure.

Along with good health, the potential diver should be a better than average swimmer. A moderately skilled swimmer can dive with SCUBA equipment, but in an emergency the swimming skills born of long practice and good physical conditioning may mean the difference between survival and death.

MAJOR CHANGES PROPOSED IN CERTIFICATION OF PHYSICIANS—

CHICAGO - Based on a forecast of the course of medical education over the next decade, the National Board of Medical Examiners has taken steps to implement long-range recommendations that call for new directions for evaluation, certification and licensure of physicians.

The ultimate objective is increased public accountability in assuring the competence of those who provide health care in this country, says an article in the current (July 23) issue of the *Journal of the American Medical Association*. Author is John P. Hubbard, M.D., of Philadelphia, president and director of the National Board of Medical Examiners.

The "new directions", Dr. Hubbard said, constitute an initial response to the conclusions and recommendations of the Committee on Goals and Priorities whose report was recently submitted to the Board. The Committee, headed by Dr. William D. Mayer, University of Missouri-Columbia School of Medicine, spent more than two years studying what Dr. Hubbard characterizes as the "complicated, disjointed and overlapping complex of medical examinations, certification and licensure" in relation

to the changing patterns of medical education.

The report, entitled "Evaluation in the Continuum of Medical Education," contains far-reaching implications for medical schools, state boards of licensure and specialty boards, according to Dr. Hubbard.

Basic changes envisioned by the Board include a single qualifying examination upon graduation from medical school which, together with the medical school's evaluation, would enable state boards to grant a permit to practice medicine under supervision during graduate education.

A full license for independent practice could then be awarded by a state board following completion of graduate medical education and specialty board certification. For those who are not certified by a specialty board, alternate prerequisites for licensure would be determined by the state boards.

Beyond completion of graduate education and entry into practice, periodic examination of professional competence leading to re-certification and perhaps re-licensure will almost certainly be required throughout the professional career of the physician. The responsibility for re-certification will rest, the National Board believes, with the agencies that grant specialty certification in the first instance, the specialty boards.

HEPATITIS IS ADDED THREAT TO ARTIFICIAL KIDNEY PATIENTS—

CHICAGO - Patients who are being kept alive on artificial kidney machines run a high risk of contracting hepatitis, studies reported in the current (July 23) issue of the *Journal of the American Medical Association*.

Hospital nurses and others working in the kidney dialysis centers also are subjected to increased hepatitis risk, often through contamination by accidental needle pricks while working with their patients.

One article, from the Center for Disease Control of the U. S. Department of Health, Education and Welfare, at Atlanta, reports on a study made in 65 kidney dialysis units across the nation. Rates of hepatitis for dialysis patients and staff were 3.3 and 3.2 cases per 100, respectively, compared with a rate of 0.03 cases per 100 population reported in the nation at large.

LISTA DE ANUNCIANTES

- | | |
|---|---------------------------------------|
| 1. Burroughs Wellcome — Empirin \bar{c} Codeine | 7. Rorer — Ascriptin |
| 2. Ciba — Vioform HC | 8. Searle — Demulen, Enovid-E, Ovulen |
| 3. Eaton Labs — Macrochantin | 9. Smith, Kline & French — Dyazide |
| 4. Geigy Pharm. — Tandearil | 10. Syntex — Neo-Mull-Soy |
| 5. Pharm. Mfrs. — Institutional | 11. Upjohn — Unicap Therapeutic |
| 6. Roche — Bactrim, Dalmane, Librium, ¹ Valium | |

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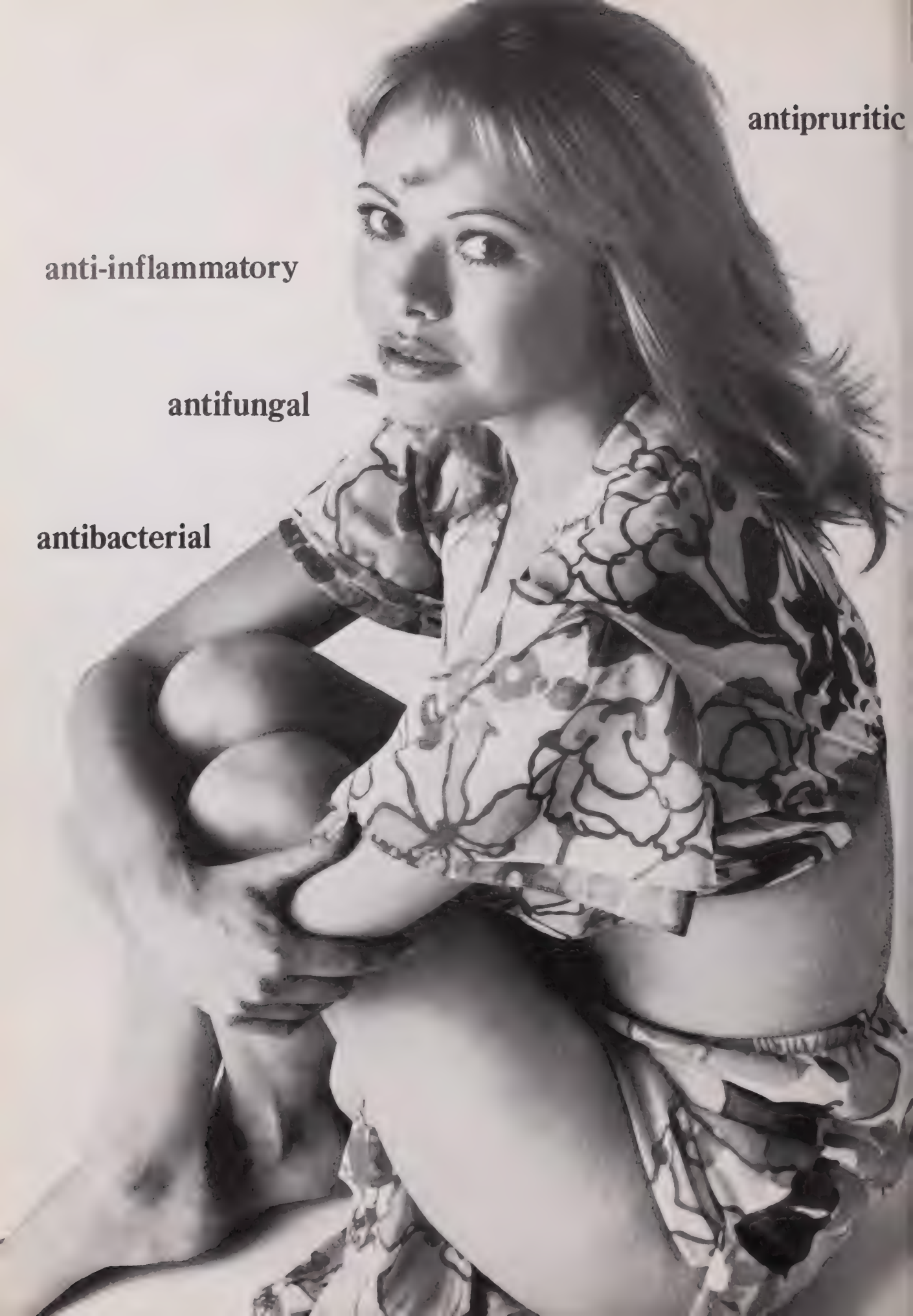
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Plain topical steroids alone are not ordinarily recommended if the skin lesion has become infected with fungi or bacteria.

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This drug has been evaluated as possibly effective for these indications. See brief prescribing information.

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INDICATIONS

Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, FDA has classified the indications as follows:

"Possibly" effective: Contact or atopic dermatitis; impetiginized eczema; nummular eczema; infantile eczema; endogenous chronic infectious dermatitis; stasis dermatitis; pyoderma; nuchal eczema and chronic eczematoid otitis externa; acne urticata; localized or disseminated neurodermatitis; lichen simplex chronicus; anogenital pruritus; (vulvae, scrota, ani); folliculitis; bacterial dermatoses; mycotic dermatoses such as tinea (capitis, cruris, corporis, pedis); moniliasis; intertrigo.

Final classification of the less-than-effective indications requires further investigation.

CONTRAINDICATIONS

Hypersensitivity to Vioform-Hydrocortisone, or any of its ingredients or related compounds; lesions of the eye; tuberculosis of the skin; active viral skin lesions (including herpes simplex, vaccinia, and molluscum).

WARNINGS

This product is not for ophthalmic use. In the presence of systemic infections, appropriate systemic antibiotics should be used.

Use in Pregnancy

Although topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use in pregnant females has not been established. Therefore, this product should not be used extensively on pregnant patients in large amounts or for prolonged periods of time.

PRECAUTIONS

May prove irritating to sensitized skin in rare cases. If this occurs, discontinue therapy. May stain.

If used under occlusive dressings or for a prolonged period, watch for signs of pituitary-adrenal axis suppression.

May interfere with thyroid function tests. Wait at least one month after discontinuance of therapy before performing these tests. The ferric chloride test for phenylketonuria (PKU) can yield a false-positive result if Vioform is present in the diaper or urine.

Prolonged use may result in overgrowth of nonsusceptible organisms requiring appropriate therapy.

ADVERSE REACTIONS

Few reports include: Hypersensitivity, local burning, irritation, pruritus. Discontinue if untoward reaction occurs. Rarely, topical corticosteroids may cause striae at site of application when used for long periods in intertriginous areas.

DOSAGE

Apply a thin layer to affected areas 3 or 4 times daily.

HOW SUPPLIED

Cream, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearyl alcohol, cetyl alcohol, stearic acid, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of 5 and 20 Gm. **Ointment**, 3% iodochlorhydroxyquin and 1% hydrocortisone in a petrolatum base; tubes of 5 and 20 Gm. **Lotion**, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearic acid, cetyl alcohol, lanolin, propylene glycol, sorbitan trioleate, polysorbate 60, triethanolamine, methylparaben, propylparaben, and perfume Flora in water; plastic squeeze bottles of 15 ml. **Mild Cream**, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a water-washable base containing stearyl alcohol, cetyl alcohol, stearic acid, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of ½ and 1 ounce. **Mild Ointment**, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a petrolatum base; tubes of ½ and 1 ounce.

Consult complete product literature before prescribing.

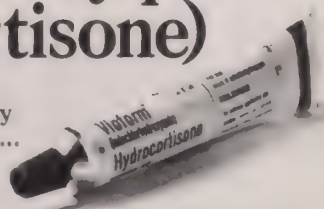
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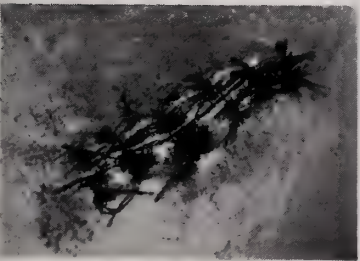
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Contraindications: Anuria, oliguria or extensive impairment of renal function is a contraindication. The drug is contraindicated for infants under one month and in pregnant patients at term. The drug should not be administered to persons who have shown hypersensitivity to nitrofurantoin.

Warnings: Macrochantin may cause hemolytic anemia of the primaquine sensitivity type, apparently linked to a glucose-6-phosphate dehydrogenase deficiency. This deficiency is found in 10 per cent of Negroes and in a small percentage of ethnic groups of Mediterranean

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Usage in pregnancy: THE SAFETY OF NITROFURANTOIN DURING PREGNANCY AND LACTATION HAS NOT BEEN ESTABLISHED. IT SHOULD NOT BE USED IN WOMEN OF CHILDBEARING POTENTIAL UNLESS THE EXPECTED BENEFITS OUTWEIGH THE POSSIBLE HAZARDS.

Precautions: Peripheral neuropathy may occur. A fatality has been reported. Predisposing conditions such as renal impairment, anemia, diabetes, electrolyte imbalance, vitamin B deficiency and debilitating disease may enhance such occurrence.

Adverse reactions: Nausea, emesis and diarrhea may occur; reduction in dosage may alleviate these symptoms. Sensitization appearing as cutaneous eruptions or pruritus has occurred. Hypersensitivity reactions resulting in nonfatal anaphylaxis, angioedema, pulmonary infiltration with pleural effusion and eosinophilia have been reported. Other possible

terial flora elsewhere in the body. (As with other antibacterials, superinfections may occur, but these are limited to the urinary tract. Pseudomonas is the organism most commonly implicated.)

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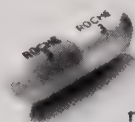
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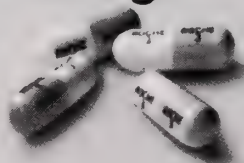
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Before prescribing, please consult complete product information, a summary of which follows:

Indications: Relief of anxiety and tension occurring alone or accompanying various disease states.

Contraindications: Patients with known hypersensitivity to the drug.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation, or in women of childbearing age require that its potential benefits be weighed against its possible hazards.

Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

Supplied: Librium® Capsules containing 5 mg, 10 mg or 25 mg chlordiazepoxide HCl. Libritabs® Tablets containing 5 mg, 10 mg or 25 mg chlordiazepoxide.

**DISPLAY
SHELVES**

JAN 9 '74

The Francis A. Countway
Library of Medicine
1015 North Street
Boston, Massachusetts 02111

Boletín

**asociación médica
de puerto rico**



Vol. 65

Noviembre 1973

No.11



Everybody experiences psychic tension.



Most people can handle this tension.



Some people develop excessive psychic tension and need your counseling



and a few may need counseling
and the psychotropic action of Valium® (diazepam).

Before deciding to make Valium (diazepam) part of your treatment plan, check on whether or not the patient is presently taking drugs and, if so, what his response has been. Along with the medical and social history, this information can help you determine initial dosage, the possibility of side effects and the ultimate prospects of success or failure.

While Valium can be a most helpful adjunct to your counseling, it should be prescribed only as long as excessive psychic tension persists and should be discontinued when you decide it has accomplished its therapeutic task. In general, when dosage guidelines are followed, Valium is well tolerated (see Dosage). For convenience it is available in 2-mg, 5-mg and 10-mg tablets.

Drowsiness, fatigue and ataxia have been the most commonly reported side effects.

Until response is determined, patients receiving Valium should be cautioned against engaging in hazardous occupations requiring complete mental alertness, such as driving or operating machinery.

JAN 9 '74

The Francis A. Countway
Library of Medicine
10 Shattuck Street
Boston, Massachusetts 02117

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindications: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

Dosage: Individualize for maximum beneficial effect.

Adults: Tension, anxiety and psychoneurotic states, 2 to 10 mg b.i.d. to q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed; adjunctively in skeletal muscle spasm, 2 to 10 mg t.i.d. or q.i.d.; adjunctively in convulsive disorders, 2 to 10 mg b.i.d. to q.i.d. **Geriatric or debilitated patients:** 2 to 2½ mg, 1 or 2 times daily initially, increasing as needed and tolerated. (See Precautions.) **Children:** 1 to 2½ mg t.i.d. or q.i.d. initially, increasing as needed and tolerated (not for use under 6 months).

Supplied: Valium® (diazepam) Tablets, 2 mg, 5 mg and 10 mg; bottles of 100 and 500. All strengths also available in Tel-E-Dose® packages of 1000.



Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, N.J. 07110

Valium® (diazepam)

To help you manage excessive psychic tension

BOLETIN

ASOCIACION MEDICA DE PUERTO RICO



Organo Oficial

Fundado en 1903

Volumen 65

Noviembre 1973

Número 11

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acute arthritic inflammation...heat that freezes

In acute rheumatoid arthritis consider Tandearil. The anti-inflammatory action of Tandearil quickly helps reduce heat, pain, swelling, and stiffness. Results are usually seen in 3 or 4 days. Try it for a week when the symptoms defy aspirin control.

Remember that Tandearil is not a simple analgesic. It should not be used on patients responding to routine therapy. Before using, please read the prescribing information. It's summarized below.

Tandearil® helps take the heat off oxyphenbutazone NF Geigy

Tablets of 100 mg.

Important Note: This drug is not a simple analgesic. Do not administer casually. Carefully evaluate patients before starting treatment and keep them under close supervision. Obtain a detailed history, and complete physical and laboratory examination (complete hemogram, urinalysis, etc.) before prescribing and at frequent intervals thereafter. Carefully select patients, avoiding those responsive to routine measures, contraindicated patients or those who cannot be observed frequently. Warn patients not to exceed recommended dosage. Short-term relief of severe symptoms with the smallest possible dosage is the goal of therapy. Dosage should be taken with meals or a full glass of milk. Patients should discontinue the drug and report immediately any sign of: fever, sore throat, oral lesions (symptoms of blood dyscrasia); dyspepsia, epigastric pain, symptoms of anemia, black or tarry stools or other evidence of intestinal ulceration or hemorrhage, skin reactions, significant weight gain or edema. A one-week trial period is adequate. Discontinue in the absence of a favorable response. Restrict treatment periods to one week in patients over sixty.

Indications: Acute gouty arthritis, rheumatoid arthritis, rheumatoid spondylitis.

Contraindications: Children 14 years or less; senile patients; history or symptoms of G.I. inflammation or ulceration including severe, recurrent or persistent dyspepsia; history or presence of drug allergy; blood dyscrasias; renal, hepatic or cardiac dysfunction; hypertension; thyroid disease; systemic edema; stomatitis and salivary gland enlargement due to the drug; polymyalgia rheumatica and temporal arteritis; patients receiving other potent chemotherapeutic agents, or long-term anti-coagulant therapy.

Warnings: Age, weight, dosage, duration of therapy, existence of concomitant diseases, and concurrent potent chemotherapeutic affect incidence of toxic reactions. Carefully instruct and observe the individual patient, especially the aging (forty years and over) who have increased susceptibility to the toxicity of the drug. Use lowest effective dosage. Weigh initially unpredictable benefits against po-

tential risk of severe, even fatal, reactions. The disease condition itself is unaltered by the drug. Use with caution in first trimester of pregnancy and in nursing mothers. Drug may appear in cord blood and breast milk. Serious, even fatal, blood dyscrasias, including aplastic anemia, may occur suddenly despite regular hemograms, and may become manifest days or weeks after cessation of drug. Any significant change in total white count, relative decrease in granulocytes, appearance of immature forms, or fall in hematocrit should signal immediate cessation of therapy and complete hematologic investigation. Unexplained bleeding involving CNS, adrenals, and G.I. tract has occurred. The drug may potentiate action of insulin, sulfonylurea, and sulfonamide-type agents. Carefully observe patients taking these agents. Nontoxic and toxic goiters and myxedema have been reported (the drug reduces iodine uptake by the thyroid). Blurred vision can be a significant toxic symptom worthy of a complete ophthalmological examination. Swelling of ankles or face in patients under sixty may be prevented by reducing dosage. If edema occurs in patients over sixty, discontinue drug.

Precautions: The following should be accomplished at regular intervals: Careful detailed history for disease being treated and detection of earliest signs of adverse reactions; complete physical examination including check of patient's weight; complete weekly (especially for the aging) or an every two week blood check; pertinent laboratory studies. Caution patients about participating in activity requiring alertness and coordination, as driving a car, etc. Cases of leukemia have been reported in patients with a history of short- and long-term therapy. The majority of these patients were over forty. Remember that arthritic-type pains can be the presenting symptom of leukemia.

Adverse Reactions: This is a potent drug; its misuse can lead to serious results. Review detailed information before beginning therapy. Ulcerative esophagitis, acute and reactivated gastric and duodenal ulcer with perforation and hemorrhage, ulceration and perforation of large bowel, occult G.I. bleeding with anemia,

gastritis, epigastric pain, hematemesis, dyspepsia, nausea, vomiting and diarrhea, abdominal distention, agranulocytosis, aplastic anemia, hemolytic anemia, anemia due to blood loss including occult G.I. bleeding, thrombocytopenia, pancytopenia, leukemia, leukopenia, bone marrow depression, sodium and chloride retention, water retention and edema, plasma dilution, respiratory alkalosis, metabolic acidosis, fatal and nonfatal hepatitis (cholestasis may or may not be prominent), petechiae, purpura without thrombocytopenia, toxic pruritus, erythema nodosum, erythema multiforme, Stevens-Johnson syndrome, Lyell's syndrome (toxic necrotizing epidermolysis), exfoliative dermatitis, serum sickness, hypersensitivity angitis (polyarteritis), anaphylactic shock, urticaria, arthralgia, fever, rashes (all allergic reactions require prompt and permanent withdrawal of the drug), proteinuria, hematuria, oliguria, anuria, renal failure with azotemia, glomerulonephritis, acute tubular necrosis, nephrotic syndrome, bilateral renal cortical necrosis, renal stones, ureteral obstruction with uric acid crystals due to uricosuric action of drug, impaired renal function, cardiac decompensation, hypertension, pericarditis, diffuse interstitial myocarditis with muscle necrosis, perivascular granulomata, aggravation of temporal arteritis in patients with polymyalgia rheumatica, optic neuritis, blurred vision, retinal hemorrhage, toxic amblyopia, retinal detachment, hearing loss, hyperglycemia, thyroid hyperplasia, toxic goiter, association of hyperthyroidism and hypothyroidism (causal relationship not established), agitation, confusional states, lethargy; CNS reactions associated with overdosage, including convulsions, euphoria, psychosis, depression, headaches, hallucinations, giddiness, vertigo, coma, hyperventilation, insomnia; ulcerative stomatitis, salivary gland enlargement.

(B)98-146-800-F (10/71)
For complete details, including dosage, please see full prescribing information.

GEIGY Pharmaceuticals
Division of CIBA-GEIGY Corporation
Ardsley, New York 10502



More than sleep.

your choice of sleep medication
is wisely based on more than
sleep-inducing potential

sleep with relative safety

Chronic tolerance studies have confirmed the relative safety of Dalmane (flurazepam HCl); no depression of cardiac or respiratory function was noted in patients administered recommended or higher doses for as long as 90 consecutive nights.

In most instances when adverse reactions were reported, they were mild, infrequent and seldom required discontinuance of therapy. Morning "hang-over" with Dalmane has been relatively infrequent. Dizziness, drowsiness, lightheadedness and the like have been the side effects noted most frequently, particularly in the elderly and debilitated. (An initial dose of Dalmane 15 mg should be prescribed for these patients.)

sleep for 7 to 8 hours without need to repeat dosage

No sleep medication has been as rigorously evaluated in the sleep research laboratory as Dalmane. Insomnia patients given one 30-mg capsule of Dalmane at bedtime, on average: fell asleep within 17 minutes, had fewer nighttime awakenings, spent less time awake after sleep onset, and slept for 7 to 8 hours with no need to repeat dosage during the night.

sleep with consistency

Dalmane (flurazepam HCl) is a distinctive sleep medication—a benzodiazepine specifically indicated for insomnia. It is not a barbiturate or methaqualone, nor is it related chemically to any other available hypnotic.

When your evaluation of insomnia indicates the need for a sleep medication, consider Dalmane—a single entity nonnarcotic, non-barbiturate agent proved effective and relatively safe for relief of insomnia.

Dalmane has been shown to be consistently effective even during consecutive nights of administration, with no need to increase dosage.

DALMANE[®]

(flurazepam HCl)

When restful sleep is indicated

One 30-mg capsule h.s. —usual adult dosage
(15 mg may suffice in some patients)

One 15-mg capsule h.s. —initial dosage for elderly or debilitated patients.

Before prescribing Dalmane (flurazepam HCl), please consult Complete Product Information, a summary of which follows:

Indications: Effective in all types of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings and/or early morning awakening; in patients with recurring insomnia or poor sleeping habits; and in acute or chronic medical situations requiring restful sleep. Since insomnia is often transient and intermittent, prolonged administration is generally not necessary or recommended.

Contraindications: Known hypersensitivity to flurazepam HCl.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. Caution against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Use in women who are or may become pregnant only when potential benefits have been weighed against possible hazards. Not recommended for use in persons under 15 years of age. Though physical and psychological dependence have not been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage.

Precautions: In elderly and debilitated, initial dosage should be limited to 15 mg to preclude oversedation, dizziness and/or ataxia. If combined with other drugs having hypnotic or CNS-depressant effects, consider potential additive effects. Employ usual precautions in patients who are severely depressed, or with latent depression or suicidal tendencies. Periodic blood counts and liver and kidney function tests are advised during repeated therapy. Observe usual precautions in presence of impaired renal or hepatic function.

Adverse Reactions: Dizziness, drowsiness, lightheadedness, staggering, ataxia and falling have occurred, particularly in elderly or debilitated patients. Severe sedation, lethargy, disorientation and coma, probably indicative of drug intolerance or overdosage, have been reported. Also reported were headache, heartburn, upset stomach, nausea, vomiting, diarrhea, constipation, GI pain, nervousness, talkativeness, apprehension, irritability, weakness, palpitations, chest pains, body and joint pains and GU complaints. There have also been rare occurrences of sweating, flushes, difficulty in focusing, blurred vision, burning eyes, faintness, hypotension, shortness of breath, pruritus, skin rash, dry mouth, bitter taste, excessive salivation, anorexia, euphoria, depression, slurred speech, confusion, restlessness, hallucinations, and elevated SGOT, SGPT, total and direct bilirubins and alkaline phosphatase. Paradoxical reactions, e.g., excitement, stimulation and hyperactivity, have also been reported in rare instances.

Dosage: Individualize for maximum beneficial effect. *Adults:* 30 mg usual dosage; 15 mg may suffice in some patients. *Elderly or debilitated patients:* 15 mg initially until response is determined.

Supplied: Capsules containing 15 mg or 30 mg flurazepam HCl



ROCHE LABORATORIES
Div., Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

It's time for action to defend the laws and regulations that protect your patients against drug substitution.

These professional and trade organizations are united in supporting antisubstitution statutes and regulations:

The American Academy of Dermatology

The Board of Directors of the
American Academy of Family
Physicians

The Executive Board of the
American Academy of Neurology

The Committee on Drugs of the
American Academy of Pediatrics

The American College of Allergists

The Executive Committee of the
American College of Obstetricians
and Gynecologists

The Board of Regents of the
American College of Physicians

The Board of Trustees of the
American Dental Association

The Board of Trustees of the
American Medical Association

The American Psychiatric Association

The Executive Committee of the
National Association of Retail
Druggists

The Board of Directors of the
Pharmaceutical Manufacturers
Association

The National Wholesale Druggists'
Association



Joint Statement on Antisubstitution Laws and Regulations

The purpose of this statement is to affirm the support of the participating organizations for the laws, regulations and professional traditions which prohibit the unauthorized substitution of drug products.

Traditionally, physicians, dentists and pharmacists have worked cooperatively to serve the best interests of patients. Productive cooperation has been achieved through mutual respect as well as a common concern for the ideals of public service. This mutual respect has been reflected, in part, by joint support over the years for the adoption and enforcement of laws and regulations specifically prohibiting unauthorized substitution and encouraging joint discussion and selection of the source of supply of drug products. The basic principles of medical, dental and pharmacy practice are thus utilized and preserved in the interest of patient welfare.

The antisubstitution laws have not obstructed enhancement of the professional status of pharmacy any more than they have in and of themselves guaranteed absolute protection from unsafe drugs, or freed physicians, dentists and pharmacists from their responsibilities to patients. As a practical matter, however, such laws and regulations encourage interprofessional communications regarding drug product selection and assure each profession the opportunity to exercise fully its expertise in drug usage, to the advantage of patients.

Physicians and dentists should be urged to increase the frequency and regularity of their contacts with pharmacists in selection of quality drug products, recognizing that

economies to patients can be improved through such communication, taking into account the patients' needs. The pharmacist's knowledge of the chemical characteristics of drugs, their mode of action, toxic properties and other characteristics that assist in making drug selection decisions should be utilized to the fullest extent practicable by physicians and dentists in serving their patients.

Since drug product selection entails knowledge derived from clinical experience, the physician's and dentist's roles in product selection remain primary and do not permit delegation of decisions requiring medical and dental judgments. A broader role in therapy will evolve for pharmacists as improved understanding and cooperation among the professions continue to grow.

There has been no evidence that there are convincing reasons to modify or repeal existing laws and regulations prohibiting the unauthorized substitution of another drug product for the one specified by a prescriber. It is our belief that such laws and regulations merit the joint support of the medical, dental and pharmaceutical professions and the pharmaceutical industry.

Add your opinion to the weight of other professionals and send it to your state assemblyman or legislator.

*Pharmaceutical Manufacturers Association
1155 Fifteenth Street, N.W., Washington, D. C. 20005*



ROCHE announces

new

BACTRIMTM

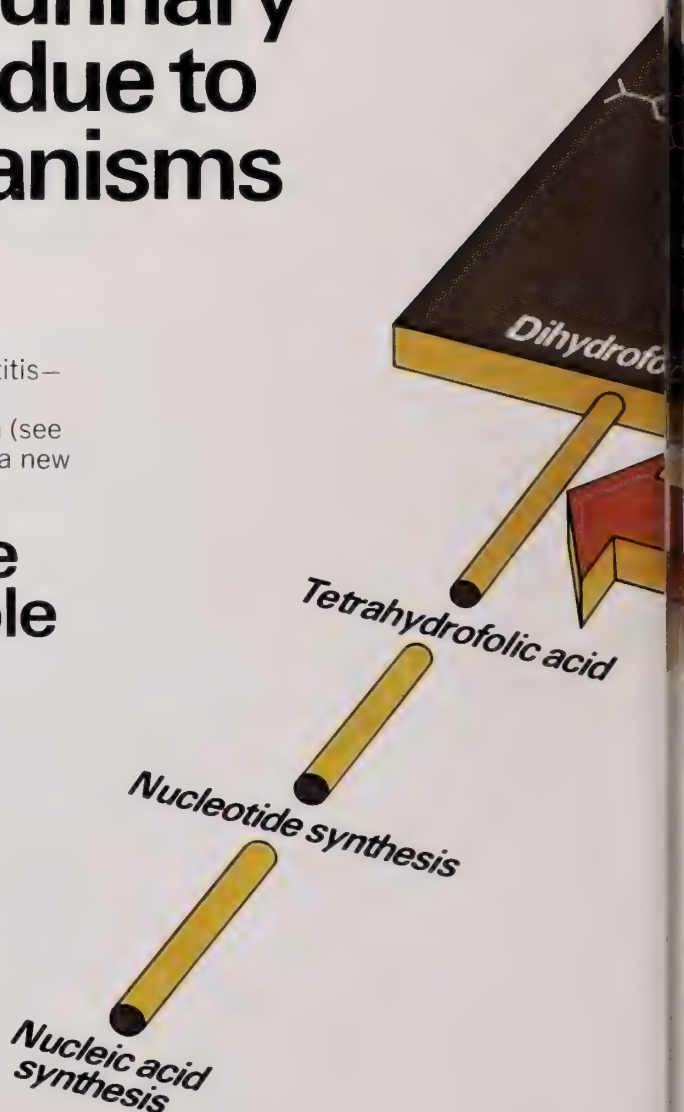
Each tablet contains 80 mg trimethoprim and 400 mg sulfamethoxazole.

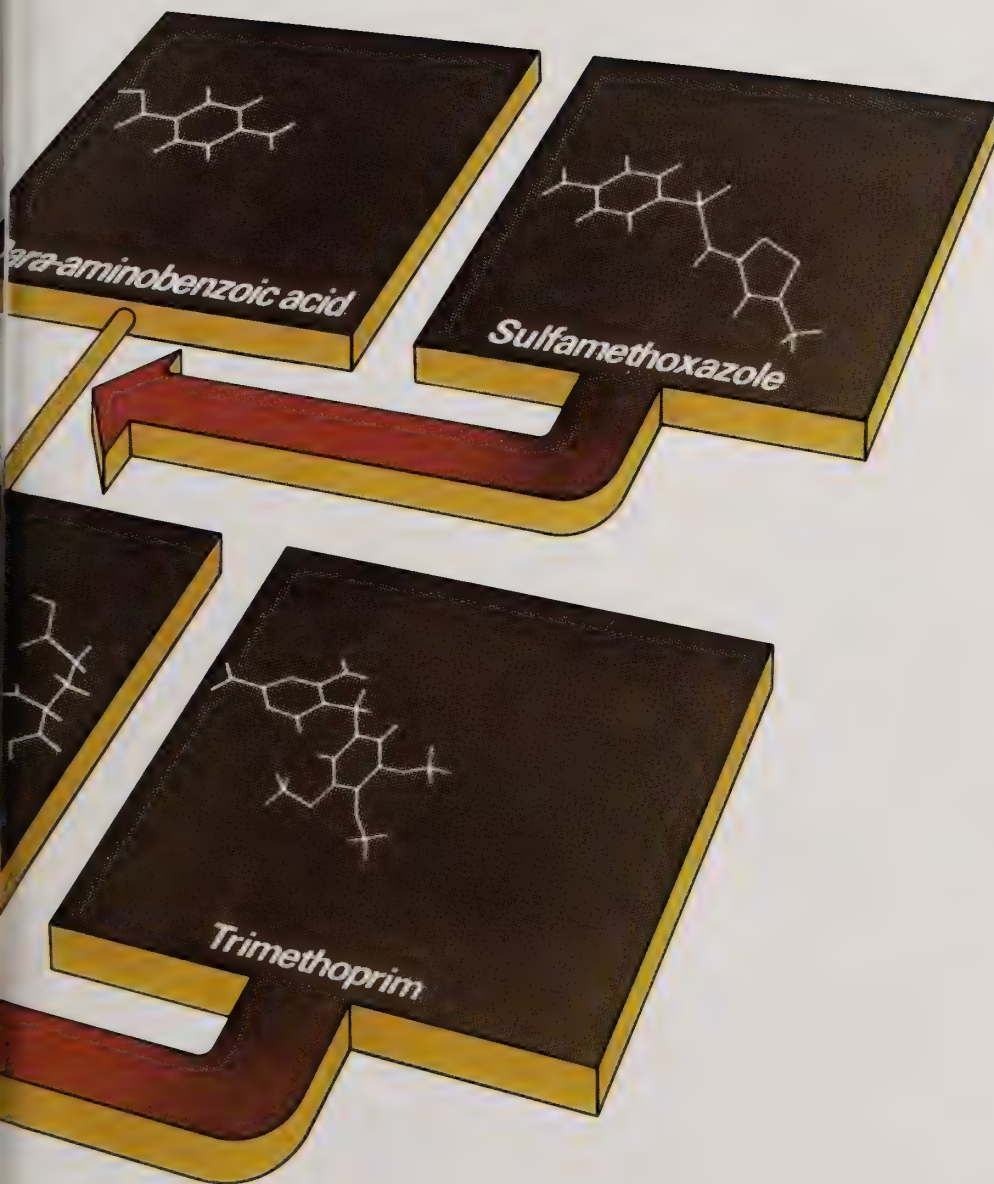
a new type of antibacterial for a two-pronged attack against chronic urinary tract infections due to susceptible organisms

Bactrim is highly effective in the treatment of these infections—primarily pyelonephritis, pyelitis and cystitis—when due to susceptible organisms. This efficacy is related to the unique mode of action against bacteria (see illustration), an action that, in effect, makes Bactrim a new type of antibacterial.

Bactrim interrupts the life cycle of susceptible bacteria

Unique mode of action interrupts the life cycle at two important points, thereby impeding the production of nucleic acids and proteins essential to these bacteria. These consecutive interruptions occur because sulfamethoxazole and trimethoprim resemble naturally existing substrates. By competitive replacement of these substrates, they inhibit further synthesis.





new **BACTRIMTM**

Each tablet contains 80 mg trimethoprim and 400 mg sulfamethoxazole.

for chronic urinary tract infections

Before prescribing, please see complete product information on last page of advertisement.

Excellent clinical response in chronic urinary tract infections even with obstructive complications

A multiclinic, double-blind study* of response to a ten-day course of therapy in 471[†] patients with chronic urinary tract infections demonstrated the superiority of Bactrim. On the 10th day after initiation of therapy, 91.7% (of 168 patients) showed significant bacteriological response to Bactrim, compared with 81.2% (of 144 patients) to trimethoprim and 64.5% (of 155 patients) to sulfamethoxazole. More than half of these patients had obstructive complications.

Excellent response maintained

Bactrim proved equally impressive in maintaining this bacteriological response. In the above study, after a ten-day course of therapy with Bactrim, 68.4% of patients with chronic urinary tract infections *maintained* response for up to 42 consecutive days, compared with 59.7% with trimethoprim and 44.4% with sulfamethoxazole. These results are particularly noteworthy considering the number of patients with obstructive complications—cases regarded as being notoriously difficult to treat.

Prescribing considerations

Clinical Limitations: Currently, the increasing frequency of resistant organisms is a limitation of the usefulness of all antibacterial agents, especially in the treatment of chronic and recurrent urinary tract infections. Not recommended for children under twelve.

Contraindications: Hypersensitivity to trimethoprim or sulfonamides. Pregnancy and during the nursing period.

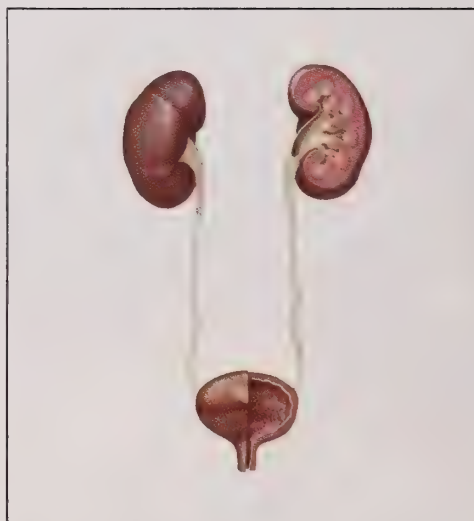
Warnings and Precautions: Both sulfamethoxazole and trimethoprim have been reported to interfere with hematopoiesis. Complete blood counts should be done frequently. If a significant reduction in the count of any formed blood element is noted, Bactrim should be discontinued. Bactrim should be given with caution to patients with impaired renal or hepatic function, possible folate deficiency, severe allergy or bronchial asthma. Maintain adequate fluid intake. Urinalyses with careful microscopic examination and renal function tests should be performed during therapy, particularly for those patients with impaired renal function.

Adverse Effects: Among the most common side effects are nausea, vomiting, rash, leukopenia and elevations in SGOT and creatinine.

Usual adult dosage: two tablets every twelve hours for 10 to 14 days; no loading dose required.

*Data on file, Hoffmann-La Roche Inc., Nutley, N.J. 07110

[†]4 patients not available for evaluation at day 10.



new **BACTRIM**TM

Each tablet contains 80 mg trimethoprim and 400 mg sulfamethoxazole.

for chronic urinary tract infections



Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, N.J. 07110

Before prescribing, please consult complete product information on facing page.

Complete Product Information:

Description: Bactrim is a synthetic antibacterial combination product, available in scored light-green tablets, each containing 80 mg trimethoprim and 400 mg sulfamethoxazole.

Trimethoprim is 2,4-diamino-5-(3,4,5-trimethoxybenzyl) pyrimidine. It is a white to light-yellow, odorless, bitter compound with a molecular weight of 290.3.

Sulfamethoxazole is *N*-(5-methyl-3-isoxazolyl)sulfanilamide. It is an almost white in color, odorless, tasteless compound with a molecular weight of 253.28.

Actions: Microbiology: Sulfamethoxazole inhibits bacterial synthesis of dihydrofolic acid by competing with *para*-aminobenzoic acid. Trimethoprim blocks the production of tetrahydrofolic acid from dihydrofolic acid by binding to and reversibly inhibiting the required enzyme, dihydrofolate reductase. Thus, Bactrim blocks two consecutive steps in the biosynthesis of nucleic acids and proteins essential to many bacteria.

In vitro studies have shown that bacterial resistance develops more slowly with Bactrim than with trimethoprim or sulfamethoxazole alone.

In vitro serial dilution tests have shown that the spectrum of antibacterial activity of Bactrim includes the common urinary tract pathogens with the exception of *Pseudomonas aeruginosa*. The following organisms are usually susceptible: *Escherichia coli*, *Klebsiella-Enterobacter*, *Proteus mirabilis* and indole-positive proteus species.

Representative Minimum Inhibitory Concentration Values for Bactrim-Susceptible Organisms (MIC—mcg/ml)				
Bacteria	Trimethoprim alone	Sulfamethoxazole alone	TMP/SMX (1:20) TMP SMX	
<i>Escherichia coli</i>	0.05—1.5	1.0 —245	0.05—0.5	0.95— 9.5
<i>Proteus</i> spp. indole positive	0.5 —5.0	7.35 —300	0.05—1.5	0.95—28.5
<i>Proteus mirabilis</i>	0.5 —1.5	7.35 — 30	0.05—0.15	0.95— 2.85
<i>Klebsiella-Enterobacter</i>	0.15—5.0	0.735—245	0.05—1.5	0.95—28.5

Human Pharmacology: Bactrim is rapidly absorbed following oral administration. The blood levels of trimethoprim and sulfamethoxazole are similar to those achieved when each component is given alone. Peak blood levels for the individual components occur one to four hours after oral administration. The half-lives of sulfamethoxazole and trimethoprim, 10 and 16 hours respectively, are relatively the same regardless of whether these compounds are administered as individual components or as Bactrim. Detectable amounts of trimethoprim and sulfamethoxazole are present in the blood 24 hours after drug administration. Free sulfamethoxazole and trimethoprim blood levels are proportionately dose-dependent. On repeated administration, the steady-state ratio of trimethoprim to sulfamethoxazole levels in the blood is about 1:20.

Sulfamethoxazole exists in the blood as free, conjugated and protein-bound forms; trimethoprim is present as free, protein-bound and metabolized forms. The free forms are considered to be the therapeutically active forms. Approximately 44 percent of trimethoprim and 70 percent of sulfamethoxazole are protein-bound in the blood. The presence of 10 mg percent sulfamethoxazole in plasma decreases the protein binding of trimethoprim to an insignificant degree; trimethoprim does not influence the protein binding of sulfamethoxazole.

Excretion of Bactrim is chiefly by the kidneys through both glomerular filtration and tubular secretion. Urine concentrations of both sulfamethoxazole and trimethoprim are considerably higher than are the concentrations in the blood. When administered together as in Bactrim, neither sulfamethoxazole nor trimethoprim affects the urinary excretion pattern of the other.

Indications: Chronic urinary tract infections (primarily pyelonephritis, pyelitis and cystitis) due to susceptible organisms (usually *E. coli*, *Klebsiella-Enterobacter*, *Proteus mirabilis*, and, less frequently, indole-positive proteus species).

Important note: Currently, the increasing frequency of resistant organisms is a limitation of the usefulness of all antibacterial agents, especially in the treatment of chronic and recurrent urinary tract infections.

Contraindications: Hypersensitivity to trimethoprim or sulfonamides. Pregnancy and during the nursing period (see Reproduction Studies).

Warnings: Deaths associated with the administration of sulfonamides have been reported from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias. Experience with trimethoprim alone is much more limited, but it has been reported to interfere with hematopoiesis in occasional patients. In elderly patients concurrently receiving certain diuretics, primarily thiazides, an increased incidence of thrombopenia with purpura has been reported.

The presence of clinical signs such as sore throat, fever, pallor, purpura or jaundice may be early indications of serious blood disorders. Complete blood counts should be done frequently in patients receiving Bactrim. If a significant reduction in the count of any formed blood element is noted, Bactrim should be discontinued.

At the present time, there is insufficient clinical information on the use of Bactrim in infants and children under 12 years of age to recommend its use.

Precautions: Bactrim should be given with caution to patients with impaired renal or hepatic function, to those with possible folate deficiency and to those with severe allergy or bronchial asthma. In glucose-6-phosphate dehydrogenase-deficient individuals, hemolysis may occur. This reaction is frequently dose-related. Adequate fluid intake must be maintained in order to prevent crystalluria and stone formation. Urinalyses with careful microscopic examination and renal function tests should be performed during therapy, particularly for those patients with impaired renal function.

Adverse Reactions: For completeness, all major reactions to sulfonamides and to trimethoprim are included below, even though they may not have been reported with Bactrim.

Blood dyscrasias: Agranulocytosis, aplastic anemia, megaloblastic anemia, thrombopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia.

Allergic reactions: Erythema multiforme, Stevens-Johnson syndrome, generalized skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis.

Gastrointestinal reactions: Glossitis, stomatitis, nausea, emesis, abdominal pains, hepatitis, diarrhea and pancreatitis.

C.N.S. reactions: Headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo, insomnia, apathy, fatigue, muscle weakness and nervousness.

Miscellaneous reactions: Drug fever, chills, and toxic nephrosis with oliguria and anuria. Periarthritis nodosa and L. E. phenomenon have occurred.

The sulfonamides bear certain chemical similarities to some goitrogens, diuretics (acetazolamide and the thiazides) and oral hypoglycemic agents. Goiter production, diuresis and hypoglycemia have occurred rarely in patients receiving sulfonamides. Cross-sensitivity may exist with these agents. Rats appear to be especially susceptible to the goitrogenic effects of sulfonamides, and long-term administration has produced thyroid malignancies in the species.

Dosage and Administration: Not recommended for use in children under 12 years of age.

The usual adult dosage is two tablets every 12 hours for 10 to 14 days.

For patients with renal impairment:

Creatinine Clearance (ml/min)	Recommended Dosage Regimen
Above 30	Usual standard regimen
15-30	2 tablets every 24 hours
Below 15	Use not recommended

How Supplied: Tablets, containing 80 mg trimethoprim and 400 mg sulfamethoxazole—bottles of 100 and 500; Tel-E-Dose® packages of 1000; Prescription Paks of 40, available singly and in trays of 10. Imprint on tablets: ROCHE 50.

Reproduction Studies: In rats, doses of 533 mg/kg sulfamethoxazole or 200 mg/kg trimethoprim produced teratological effects manifested mainly as cleft palates. The highest dose which did not cause cleft palates in rats was 512 mg/kg sulfamethoxazole or 192 mg/kg trimethoprim when administered separately. In two studies in rats, no teratology was observed when 512 mg/kg of sulfamethoxazole was used in combination with 128 mg/kg of trimethoprim. However, in one study, cleft palates were observed in one litter out of 9 when 355 mg/kg of sulfamethoxazole was used in combination with 88 mg/kg of trimethoprim.

In rabbits, trimethoprim administered by intubation from days 8 to 16 of pregnancy at dosages up to 500 mg/kg resulted in higher incidences of dead and resorbed fetuses, particularly at 500 mg/kg. However, there were no significant drug-related teratological effects.

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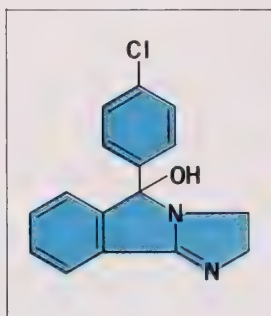
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A short-term adjunct in the treatment of exogenous obesity

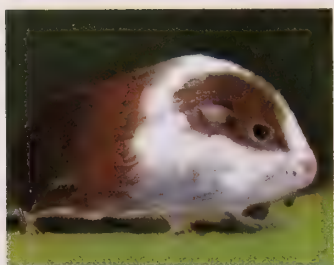
Sanorex is indicated in the management of exogenous obesity as a short-term (a few weeks) adjunct in a regimen of weight reduction based on caloric restriction. When diet and counseling are felt to be insufficient, the addition of Sanorex to the regimen may prove helpful.

Unique chemical structure among anorexiant

Sanorex (mazindol) is an imidazo-isindole anorexiant chemically unrelated to amphetamine and other sympathomimetic phenethylamines. Chemically designated as 5-p-chlorophenyl-5-hydroxy-2,3-dihydro-5H-imidazo [2,1-a] isindole, it has the following structure.



Some pharmacologic similarities to amphetamines... and some differences



Sanorex has pharmacologic activity similar in many ways to that of amphetamines, including central nervous system stimulation in humans and animals, as well as such amphetamine-like effects in animals as the production of stereotyped behavior. Animal experiments also suggest certain differences from amphetamines.

1) Site of Action—Limbic System vs. Hypothalamus

In animal experiments, Sanorex appears to exert its primary effects on the limbic system of the brain, whereas amphetamine acts upon hypothalamic and midbrain structures.*

2) Effect on Norepinephrine

Unlike amphetamine, Sanorex does not cause depletion of brain norepinephrine in animals;* on the other hand, it does appear to inhibit storage-site uptake of norepinephrine as is suggested by its marked potentiation of the effect of exogenous norepinephrine on blood pressure in dogs and on smooth muscle contraction *in vitro*.

*The significance of these differences for humans is uncertain.

Clinical studies of weight loss with Sanorex (mazindol)

The average magnitude of increased weight loss of drug-treated patients over placebo-treated patients in studies of anorexiant in general is ordinarily only a fraction of a pound a week. In clinical studies of Sanorex, the average weight loss per week for Sanorex over placebo is significant. The rate of weight loss is greatest in the first weeks of therapy for both drug and placebo subjects and tends to decrease in succeeding weeks.

Double-blind clinical trials were conducted with a total of 3858 patients, 2183 of these receiving Sanorex on varying dosage schedules. In these studies, 587 patients received Sanorex for a period of 6 weeks in recommended dosages (462 patients, 1 mg. t.i.d. and 125 patients, 2 mg. o.d.) and 451 patients received placebo.

While the weight loss associated with Sanorex has been generally consistent within individual clinical trials, the amount varies, as with other agents from trial to trial. This variance appears to be related in part to variables other than the agent prescribed, such as the interaction between physician-investigator and the patient, the population treated, and the diet prescribed. The importance of nondrug factors in such weight loss has not been elucidated.

Simplicity of dosage helps patients follow regimen

One 2-mg. tablet per day taken one hour before lunch. That's it. This one-a-day dosage can help many patients—who might otherwise tire of and become discouraged with a regimen.

Administration is flexible, however. For the patient in whom it is preferred, 1-mg. 3 times daily, one hour before meals, may be prescribed. Sanorex is supplied as 2-mg. scored tablets to facilitate these regimens.

Rx _____
*Sanorex Tablets
#40
1 Tablet one hour
before lunch*

Tolerance and dependence

Sanorex shares important pharmacologic properties with amphetamines. Amphetamines and related stimulant drugs have been extensively abused and can produce tolerance and severe psychologic dependence. In this regard, the manifestations of chronic overdosage or withdrawal of Sanorex have

not been determined in humans. Abstinence effects have been observed in dogs after abrupt cessation for prolonged periods. There was some self-administration of the drug in monkeys. While the abuse potential of Sanorex has not been clearly defined, the possibility of dependence should be kept in mind when evaluating the desirability of including Sanorex as part of a weight-reduction program.

Indication: In exogenous obesity, as a short-term (a few weeks) adjunct in a weight-reduction regimen based on caloric restriction. The limited usefulness of agents of this class should be measured against possible risk factors.

Contraindications: Glaucoma; hypersensitivity or idiosyncrasy to the drug; agitated states; history of drug abuse; during, or within 14 days following, administration of monoamine oxidase inhibitors (hypertensive crises may result.)

Warnings: Tolerance to many anorectic drugs may develop within a few weeks; if this occurs, do not exceed recommended dose, but discontinue drug. May impair ability to engage in potentially hazardous activities, such as operating machinery or driving a motor vehicle, and patient should be cautioned accordingly.

Drug Interactions: May decrease the hypotensive effect of guanethidine; patients should be monitored accordingly. May markedly potentiate pressor effect of exogenous catecholamines; if a patient recently taking mazindol must be given pressor amine agents (e.g., levarterenol or isoproterenol) for shock (e.g., from a myocardial infarction), extreme care should be taken in monitoring blood pressure at frequent intervals and initiating pressor therapy with a low initial dose and careful titration.

Drug Dependence: Mazindol shares important pharmacologic properties with amphetamines and related stimulant drugs that have been extensively abused and can produce tolerance and severe psychologic dependence. Manifestations of chronic overdose or withdrawal with mazindol have not been determined in humans. Abstinence effects

have been observed in dogs after abrupt cessation for prolonged periods. There was some self-administration of the drug in monkeys. EEG studies and "liking" scores in human subjects yielded equivocal results. While the abuse potential of mazindol has not been further defined, possibility of dependence should be kept in mind when evaluating the desirability of including the drug in a weight-reduction program.

Usage in Pregnancy: In pregnancy or women who may become pregnant, potential benefit must be weighed against possible hazard to mother and infant.

Usage in Children: Not recommended for use in children under 12 years of age.

Precautions: Insulin requirements in diabetes mellitus may be altered. Smallest amount of mazindol feasible should be prescribed or dispensed at one time to minimize possibility of overdose. Use cautiously in hypertension, with monitoring of blood pressure; not recommended in severe hypertension or in symptomatic cardiovascular disease including arrhythmias.

Adverse Reactions: Most commonly, dry mouth, tachycardia, constipation, nervousness, and insomnia. **Cardiovascular:** Palpitation, tachycardia. **Central Nervous System:** Overstimulation, restlessness, dizziness, insomnia, dysphoria, tremor, headache, depression, drowsiness, weakness. **Gastrointestinal:** Dryness of mouth, unpleasant taste, diarrhea, constipation, nausea, other gastrointestinal disturbances. **Skin:** Rash, excessive sweating, clamminess. **Endocrine:** Impotence, changes in libido have rarely been observed. **Eye:** Long-term treatment with high doses in dogs resulted in some corneal opacities, reversible on cessation of medication; no such effect has been observed in humans.

Dosage and Administration: One 2-mg. tablet per day one hour before lunch, or one-half tablet (1 mg.) three times daily one hour before meals.

How Supplied: Tablets, 2 mg., in packages of 100.

Before prescribing or administering, see package circular for Prescribing Information.



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RUBELLA SUSCEPTIBILITY AMONG PUERTO RICAN MOTHERS

E. Robert Greenberg, MD

Paul A. Blake, MD

Barnett L. Cline, MD

Kenneth L. Herrmann, MD

In most continental areas studied, more than 80 percent of the women of child-bearing age have naturally acquired rubella antibodies (1, 2). However, serologic surveys of adult women on the tropical islands of Trinidad, Jamaica, Hawaii, and Bermuda (1, 2, 3, 4, 5, 6) show that about 50 percent have rubella antibodies. In a preliminary survey, similar low immunity rates were found among adults in an urban area of Puerto Rico (7). To further define the prevalence of rubella immunity in Puerto Rico, we tested mothers from an urban area and from a rural area for rubella antibodies.

Materials and Methods

San Juan, the capital city of Puerto Rico, has a population of more than 450,000. The San Juan mothers tested in this study lived in a low socioeconomic area representative of the inner city.

The town of Aguas Buenas is located in the low mountains 24 kilometers south of metropolitan San Juan and has a population of about 3,400.

All mothers of first-grade children in an urban San Juan school district and in the Aguas Buenas elementary school were asked to participate in this study of rubella immunity. We drew venous blood specimens in November 1970, and tested the sera for rubella hemagglutination inhibition (HI) antibodies by the CDC Standardized Rubella HI technique (8). A rubella HI antibody titer of 8 or greater was considered evidence of immunity due to past infection with rubella virus.

Results

Ninety-eight women from San Juan and 93 women from Aguas Buenas participated in the study, representing about 35 percent cooperation in San Juan and 80 percent cooperation in Aguas Buenas. Of these 191

women, only 99, or 52 percent, had rubella antibodies. Table I shows the distribution of the seropositives by age of the women. Immunity rates do not differ significantly by age groups, nor do the immunity rates of urban mothers and rural mothers.

The geometric mean titers of the urban and the rural women were essentially the same (Table II). Age had no effect on the titers.

Discussion

We have encountered a low rate of rubella seropositivity among Puerto Rican women, similar to rates reported from women on other tropical islands. The population sample studied was not necessarily representative of all urban and rural women in Puerto Rico and, therefore, generalization based on our results should be attempted cautiously.

We have no satisfactory explanation for the low rates of immunity to rubella observed in Puerto Rico and the other tropical islands. Geographic isolation seems an unlikely explanation. Even though large numbers of travelers coming into San Juan provide many opportunities for introduction of rubella virus, the rate of rubella immunity for the San Juan mothers tested was low. Further, it was not significantly different from the rate for mothers tested from Aguas Buenas, a rural area, where virus introduction would be expected to be far less common.

In Puerto Rico there has been at least one epidemic of rubella, occurring in 1964 and 1965, which was followed by a sharp increase in the reported number of children born with congenital rubella syndrome (Unpublished statistics, Puerto Rico Health Department, Division of Communicable Disease Control). The Island is heavily populated, with 2.7 million people in an area less than 3,500 square miles. Given this dense population, a high rate of susceptibility to rubella, and frequent opportunities for introduction of rubella, what has prevented the virus from infecting more people through epidemic spread? We do not have the answer, and further investigations are needed.

From the San Juan Tropical Disease Laboratories, Ecological Investigations Program, Center for Disease Control, Health Services and Mental Health Administration, Public Health Service, U. S. Department of Health, Education, and Welfare, San Juan, Puerto Rico.

TABLE I: AGE DISTRIBUTION OF RUBELLA IMMUNITY IN MOTHERS FROM AGUAS BUENAS AND SAN JUAN, PUERTO RICO — 1970

Age Group	Number Tested	San Juan		Number Tested	Aguas Buenas	
		Number Immune *	Percent Immune		Number Immune *	Percent Immune
20-29	51	25	49	33	19	58
30-39	32	13	41	40	21	53
40-49	15	9	60	20	12	60
Total	98	47	48	93	52	56

* - Rubella HI titers 8 or greater, expressed as the reciprocal of the dilution.

TABLE II: GEOMETRIC MEAN RUBELLA HI TITERS FOR SEROPOSITIVE MOTHERS FROM SAN JUAN AND AGUAS BUENAS BY AGE

Age Group	Geometric Mean Titer *	
	San Juan	Aguas Buenas
20-29	49	46
30-39	30	48
40-49	60	39
Total	44	45

* - Expressed as the reciprocal of the dilution.

Summary

We tested a group of urban women and a group of rural women in Puerto Rico for rubella HI antibodies. The overall prevalence of rubella antibody was 52 percent. There was no significant difference in antibody rates nor in geometric mean antibody titers between the urban and rural groups. The exceptionally low prevalence of rubella immunity is similar to that reported on several other tropical islands.

Resumen

Hemos examinado un grupo de mujeres de la zona

urbana y un grupo de mujeres de la zona rural en Puerto Rico para detectar anticuerpos a rubella en la prueba de HI (Inhibición de Hema-aglutinación). La prevalencia general a anticuerpos de rubella fue de 52 por ciento. No hubo diferencia significativa en la tasa de anticuerpos, ni en el promedio geométrico de los títulos de anticuerpos entre la zona rural y urbana. La prevalencia excepcionalmente baja de inmunidad a rubella es similar a la reportada en varias islas tropicales.

Acknowledgments

The cooperation of the health educators of the Puerto Rico Department of Education greatly facilitated this study.

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PRIMARY DRUG RESISTANT TUBERCULOSIS IN PUERTO RICO

Michael B. Zack, MD
Ramón E. Figueroa-Lebrón, MD, FCCP

Sensitivity studies of mycobacterial cultures are very important for several reasons. (1) In the face of clinical disease responding slowly or not at all to customary chemotherapy, the therapeutic regimen may be evaluated in the light of drug sensitivity studies and more specific regimens instituted. (2) From an epidemiologic and surveillance standpoint, especially in the poorer countries of the world, the presence of resistant organisms serves as a marker of unsuccessful therapy, due to the doctor and/or the patient's fault. (3) In previously untreated patients, the presence of resistant organisms (hence primary drug resistance) is a useful index for observing changes in the incidence of primary drug resistant organisms and hence possible biological changes in the organism itself. (4) From a public health standpoint, a high incidence of resistant organisms should alert public health officials and all other tuberculosis workers, that incorrect management of tuberculous disease may be occurring and nurturing the emergence of these resistant strains.

With these objectives in mind, sensitivity studies were performed on all positive *Mycobacterium* cultures at the Veterans Administration Hospital, San Juan, Puerto Rico.

Methods

Every culture positive for *Mycobacterium tuberculosis* during the period June, 1970 to February, 1972 was evaluated. There were 45 such niacin-positive *M. tuberculosis* cultures. The medium used was Lowenstein-Jensen. Indirect drug susceptibility testing was performed on all 45 specimens (1). The organism to be tested was inoculated onto 7H-9 media and incubated for seven days until it was a turbid as MacFarland No. 1 standard. It was then diluted with sterile saline, and pipette inoculated into quadrants of drug and control media. Plates were placed medium down in polyethylene plastic bags,

sealed, incubated in 5-10 percent CO₂ at 35-37°C. They were read in 2 to 3 weeks using a dissecting microscope (30-60X total magnification). The bacterial growth on control and drug media was recorded as follows:

4 plus: confluent growth (500 or more colonies) ¹
3 plus: 200-500 colonies
2 plus: 50-100 colonies
1 plus: 50-100 colonies
Less than 50 colonies: actual count

Control discs had no drug added and represented untreated organism growth.

The drug concentrations used were as follows:

INH	0.2 mcg/ml
Streptomycin (SM)	2.0 mcg/ml
PAS	2.0 mcg/ml
Kanamycin (KY)	5.0 mcg/ml
Ethionamide (ETA)	5.0 mcg/ml
Ethambutol (EMB)	5.0 mcg/ml
Cycloserine (CS)	50.0 mcg/ml

The clinical records of all those patients having any drug resistant organisms were examined to determine if they had ever received antituberculous chemotherapy before. If they had, they were classified as secondary drug resistance. If they had not, they were classified as primary drug resistance.

Results

There were 45 positive cultures for *M. tuberculosis* during the period of the study. All were included. 3 of the 45 (7 percent) had organisms totally sensitive to each of the seven drugs tested. Forty two of the 45 (93 percent) had organisms resistant to one or more of the 7 drugs. Thirty two of the group (71 percent) had been previously treated for tuberculosis with one or more of the antituberculous drugs. They are thus presumably a population with acquired drug resistant organisms. There were 10 patients of the 45 (22 percent) who had never had antituberculous therapy, whose organisms were resistant to 1 or more drugs, and who therefore had primary drug resistant organisms.

None of these ten had been in countries other than the U. S.

Two of these had carcinoma of the neck, treated with radiotherapy, before the emergence of primary drug resistant TB. Their cases are briefly presented below. Two other cases of primary drug resistance,

From the Dept. of Medicine (Pulmonary Unit), Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts and the Pulmonary Function Laboratory and Inhalation Therapy Service, VA Hospital, San Juan, Puerto Rico.



Fig. 1: Case 1 (Pt. F. E.) Initial chest film of patient with primary drug resistant tuberculosis of slight degree. Treatment was begun in the face of drug resistance.



Fig. 2: Case 1 (Pt. F. E.) Chest film after seven months of therapy with drugs to which the organism was slightly resistant. Significant clearing of the right upper lung field infiltrate has occurred.

one an example of changing the original drug regimen, and the other an example of continuing with it, are presented.

CASE 1: F. E. 62-year old diabetic with cough, fever, weakness and positive sputum for *M. tuberculosis*. Chest film showed a right lung infiltrate. He was treated with INH (300 mg), SM (1 gm), and EMB (1200 mg). Sensitivity studies showed 1 + resistance to INH, 2 + to ETA and CS, 1 + to KM, 4 colonies to EMB, and 13 colonies to SM. On this therapy he converted his sputum to negative three months later, and has continued to improve, including an 18 lb. weight gain. Fig. 1 shows his chest film on admission, and Fig. 2 his chest film after therapy.

CASE 2: M. S. 49-year old admitted with a right upper lobe cavity and a positive culture for *M. tuberculosis*. He was initially treated with INH, PAS, and SM, but on the basis of sensitivity studies the INH was discontinued and ETA begun. His therapy was finally ETA (250 mg BID), PAS (3 gms QID), and SM (1 gm). His organism showed 4 + resistance to EMB and CS, and 35 colonies to INH. He quickly converted

his sputum to negative and clinically improved. His admission film is shown in Fig. 3 and his post therapy film in Fig. 4.

CASE 3: A. P. 35-year old with carcinoma of the larynx treated with radiotherapy (3000rads) to the neck. While receiving therapy, positive sputum for AFB was obtained which was 4 + resistant to EMB and CS, and had 11 colonies to INH. He was treated with INH, EMB, SM, and after obtaining the sensitivities ETA was substituted for the EMB. He died and at post-mortem exam showed diffuse metastatic disease.

CASE 4: R. F. 48-year old with carcinoma of the neck and mouth, treated extensively with radiotherapy. An incidental finding was a positive AFB culture with organisms resistant to INH (3 +) SM (2 +), and minimally to CS. He was treated with INH, EMB, and ETA, and died of metastatic disease.

Discussion

The recognition of organisms resistant to antituber-



Fig. 3: Case 2 (Pt. M. S.) Initial chest film of patient with primary drug resistant tuberculosis of moderate degree. Treatment was begun with alternate drugs on the basis of drug sensitivities.



Fig. 4: Case 2 (Pt. M. S.) Chest film after 5 months of therapy with drugs to which the organism was sensitive. Significant interval clearing in the right lung has occurred.

culous drugs guides physicians in judicious management of these patients with more specific drugs, permits monitoring of the incidence of such resistant strains, and most importantly, serves as an admonition. All too frequently resistant organisms signify failure: of the patient to take his medication properly, of the physician to prescribe adequate therapy, or both. With an incorrect dosage, or use of too few drugs, the physician is abetting and nurturing the emergence of resistant strains. Such a patient becomes a case of acquired drug resistance. When he transmits his disease to an uninfected person, he is transmitting drug-resistant organisms. This latter patient then becomes a case of primary drug resistant TB. Yet the responsibility for this latter patient still lies with the physician's incorrect management of the former patient.

These preliminary results demonstrate that 93 percent of all the strains were resistant to one or more of the anti-TB drugs and that 32/45 (71 percent) were retreatment cases. The 10 patients who had primary drug resistant organisms, represent the unfortunate innocent bystanders: people who are infected by the

incorrectly managed or medically irresponsible patients under treatment. A third possibility exists: that chance genetic mutation in wild strains independent of exposure to these midmanaged cases, is responsible for the resistant organisms. We can neither prove nor disprove this here.

The incidence of primary drug resistance (INH) in the US is about 3 percent (2). In our patients the incidence was considerably higher although the level of resistance was of a small magnitude and perhaps below the level of clinical significance (3). Our 3 cases of 4 + EMB resistance constitute a 6.6 percent primary resistance level to this drug, which more and more is being used as part of the initial chemotherapeutic regime. This high incidence of primary EMB resistance is in accord with the findings of others (2). Eight of the 45 patients (18 percent) had primary drug resistance to CS. Similarly the large number of patients (eight) in this series with primary drug resistance to two or more drugs, constitutes an indication for sensitivity studies in the treatment of TB patients from Puerto Rico, if judicious and specific

chemotherapy is anticipated.

In less developed countries the percentage of resistant organisms rises to levels of 25 percent or greater in parts of Africa and Asia (4). American soldiers returning home from Vietnam have recently been observed to introduce into the American population the high level of primary resistance encountered in Vietnam (5).

The potentially tragic consequences of drug-resistant organisms have been well described in a family outbreak in New York and the importance of sensitivity surveillance stressed (6).

The representative cases illustrate several important points. Case 1, F. E. showed resistance to INH, ETA, CS, KY, and slightly to SM. His therapy (INH, SM, EMB) was given and continued in the face of 1 + INH resistance, EMB sensitivity, and minimal SM resistance. After 3 months he converted his culture and improved dramatically. The radiographic improvement is corroborative of his clinical course. The case points out that homologous treatment can be carried out in the face of organisms slightly resistant (*in vitro*) to these drugs with excellent results. However, such a procedure demands and requires very close and careful monitoring of the patient and of his sputum's bacteriologic characteristics.

Case 2, M. S. had his treatment changed on the basis of his sensitivity pattern. His clinical improvement was also accompanied by dramatic radiographic improvement. This case illustrates the judicious use of alternative chemotherapy on the basis of sensitivity studies. In this patient, INH (35 colonies) and EMB (4 + resistance) treatment alone might have been disastrous.

Cases 3 and 4 had neck carcinoma. Both had received intensive radiotherapy prior to the emergence of their primary drug resistant TB, radiation may have induced a genetic mutation in the tubercle bacilli which resulted in the expression of primary drug resistance. We have no data to support or disprove this, but it is perhaps an interesting area for further investigation.

It is especially fitting at the beginning of a Rifampin era in chemotherapy to raise the question of judicious anti-tuberculous drug use. Clearly the case for awareness of drug resistance in TB is a case for proper and intelligent initial treatment. This is one area where a little treatment may indeed be worse than none at all.

Summary

Drug sensitivity studies were performed on 45 positive *M. tuberculosis* cultures at the San Juan, Puer-

to Rico VA Hospital, and 94 percent of the organisms showed resistance to one or more of the anti-tuberculous drugs tested. Most of these were in patients previously treated for tuberculosis. But in ten patients (22 percent) lack of previous treatment indicated primary drug resistance. Of interest was a very high degree of resistance to Cycloserine, and an absolute resistance to Ethambutol in several patients.

Previous administration of radiotherapy in 2 of the 10 patients raised the question of radiation-induced mutation in the organism expressing itself as drug resistance.

Representative cases illustrate the therapeutic implications of drug sensitivity testing.

The higher than expected incidence of primary drug resistance is a reflection in part of acquired drug resistance in the community which in turn is a reflection of patients not properly taking medication and/or physicians improperly prescribing it.

Because of the high influx of Puerto Rican patients to the mainland, and viceversa, these data are of relevance to American physicians and public health officials.

Resumen

Estudios de sensibilidad a drogas fueron hechos en 45 cultivos positivos para tuberculosis en el Hospital de Veteranos de Puerto Rico. Noventa y cuatro por ciento (94 por ciento) de los organismos demostraron resistencia a una o más de las drogas antituberculosas. La mayor parte de estos cultivos procedían de pacientes con tratamiento previo para tuberculosis pero en diez de los pacientes veinte y dos por ciento (22 por ciento) no había indicio de tratamiento previo indicando así resistencia primaria.

Es de especial interés el alto grado de resistencia a cicloserina y una resistencia absoluta a Myambutol en ciertos pacientes.

La previa administración de radioterapia a dos pacientes de los diez que demostraron resistencia primaria levanta la cuestión si una mutación causada por la radioterapia fue la causa de la resistencia primaria.

Los casos representativos ilustran las diferentes implicaciones terapéuticas y las ventajas de probar la sensibilidad a drogas.

La incidencia mayor que la esperada de resistencia primaria es un reflejo en parte de resistencia adquirida en la comunidad que a su vez refleja que los pacientes no están recibiendo la medicación adecuadamente o que

se le está prescribiendo la medicación adecuadamente.

Debido a la importancia pública de una incidencia tan alta de resistencia primaria a drogas se llamó la atención hacia esta situación.

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Usage in pregnancy: Weigh the potential benefits against possible risks before using during pregnancy, lactation or in women of childbearing age. Diphenoxylate HCl and atropine are secreted in the breast milk of nursing mothers.

Precautions: Addiction (dependency) to diphenoxylate HCl is theoretically possible at high dosage. Do not exceed recommended dosages. Administer with caution to patients receiving addicting drugs or known to be addiction prone or having a history of drug abuse. The subtherapeutic amount of atropine is added to discourage deliberate overdosage; strictly observe contraindications, warnings and precautions for atropine; use with caution in children since signs of atropinism may occur even with the recommended dosage.

Adverse reactions: Atropine effects include dryness of skin and mucous membranes, flushing and urinary retention. Other side effects with Lomotil include nausea, sedation, vomiting, swelling of the gums, abdominal discomfort, respiratory depression, numbness of the extremities, headache, dizziness, depression, malaise, drowsiness, coma, lethargy, anorexia, restlessness, euphoria, pruritus, angioneurotic edema, giant urticaria and paralytic ileus.

Dosage and administration: Lomotil is contraindicated in children less than 2 years old. Use only Lomotil liquid for children 2 to 12 years old. For ages 2 to 5 years, 4 ml. (2 mg.) t.i.d.; 5 to 8 years, 4 ml. (2 mg.) q.i.d.; 8 to 12 years, 4 ml. (2 mg.) 5 times daily; adults, two tablets (5 mg.) t.i.d. to two tablets (5 mg.) q.i.d. or two regular teaspoonfuls (10 ml., 5 mg.) q.i.d. Maintenance dosage may be as low as one fourth of the initial dosage. Make downward dosage adjustment as soon as initial symptoms are controlled.

Overdosage: Keep the medication out of the reach of children since accidental overdosage may cause severe, even fatal, respiratory depression. Signs of overdosage include flushing, lethargy or coma, hypotonic reflexes, nystagmus, pinpoint pupils, tachycardia and respiratory depression which may occur 12 to 30 hours after overdose. Evacuate stomach by lavage, establish a patent airway and, when necessary, assist respiration mechanically. Use a narcotic antagonist in severe respiratory depression. Observation should extend over at least 48 hours.

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CLINICAL EXPERIENCE WITH EUTHROID: *A New Drug for Thyroid Replacement Therapy*

Francisco Aguiló, Jr., MD

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The principal aim of endocrine replacement therapy is to return the patient to his eu-hormonal state, characterized by the absence of symptoms and signs indicative of either hyper- or hypo-function of that particular hormone. This is usually accomplished by supplying the amount of hormone that a normal individual would be expected to produce.

Hypothyroidism is one of the easiest deficiencies to treat, only complicated by limitations imposed by the patient's cardiovascular status and the quality and potency of the thyroid preparation employed.

The potency of different thyroid preparations has been a matter of concern. Some batches of desiccated animal thyroid have been found to be biologically inactive, while still meeting the rather obsolete USP requirements based on their iodine content (1 - 8). The addition of bioassay on such preparation has proven helpful in detecting and controlling the problem, but the use of synthetic preparations of either levo- thyroxine (T4) or levo-triiodothyronine (T3) can best assure the accuracy of dosification.

The end-point of such therapy must ultimately be judged subjectively by the patient and objectively by the trained clinician, who can best decide whether or not the patient has been rendered euthyroid. There are instances, however, when the patient's reliability is questionable, or that concomittant medical problems obscure the usual clinical criteria. Under such circumstances it is desirable to have additional means of further evaluating the patient's state of thyroid replacement, such as laboratory studies. Among the latter, serum

cholesterol and plasma protein-bound iodine (PBI) have long enjoyed acceptance, even to the point of abusive over-dependence.

The use of synthetic T3 and T4 preparations determine changes in the plasma PBI levels, imposed by their relative affinity for plasma protein carriers. Thus, the marked affinity of T4 for thyroxine binding globulin (TBG) results in higher than expected PBI's and conversely, the poor binding of T3 to TBG accounts for its more rapid disposal and lower PBI's than the patient's clinical status would suggest. It would seem advantageous to employ preparations that could correlate plasma PBI and clinical status as closely as possible. The obvious solution would be to combine T3 and T4 in their usual physiologic proportions. Animal studies suggest that such T4/T3 ratio varies from 2:1 to 4.5:1 (4-5). Experimentally a 4:1 ratio seems to best mimic the in vivo hormonal needs and to correlate with normalcy of laboratory parameters (7-9).

This report is concerned with our experience in the original clinical evaluation of a new thyroid preparation* having such a ratio. Its therapeutic efficacy, dosification and its effect on plasma PBI, serum cholesterol and other parameters have been evaluated.

Materials and Methods

Thirty patients with hypothyroidism were selected at random from among those attending the Medicine and Endocrine Clinics of the University District Hospital (Table I). Twelve were receiving thyroid replacement therapy, while 18 had never been treated. Their ages ranged from 15 to 70 with a mean of 30.4 years. There were 20 females and 10 males. Duration of their disease varied from 1 month to 22 years (mean 5.4 years) (Table II). All but one had primary hypothyroidism, most commonly idiopathic (Table III). Severity varied from mild to severe and 4 were euthyroid at the beginning of Euthroid therapy (Table II).

A detailed history, a complete physical examination, pertinent X-ray films, ECG and laboratory studies were performed before starting Euthroid and at 1 - 2 months intervals, as per a

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* - Euthroid (Liotrix) supplied by the Warner Lambert Research Institute, Morris Plains, New Jersey as W-1782.

TABLE I: PATIENT PROFILE

Age Range	15 - 70 yrs.	Mean : 30.4
Sex	Female: 20	Male : 10
Duration of Disease	1 mo. - 22 yrs.	(Mean: 5.4 yrs.)
Etiology	Primary: 29	Secondary: 1
Previously treated	12	Untreated: 18
Severity of disease	Euthyroid to severely hypothyroid	

TABLE II: DURATION OF HYPOTHYROIDISM

Severity *	No. Patients	Range	Mean
Euthyroid	4	6 - 17 yrs.	13.0 yrs.
Mild hypo	8	1 mo. - 8 yrs.	3.5
Mod. severe	6	8 mo. - 22 yrs.	5.0
Severe	12	8 mo. - 17 yrs.	4.4
Total	30	1 mo. - 22 yrs.	5.4 yrs.

* - At time of beginning Euthroid therapy.

TABLE III: ETIOLOGY OF HYPOTHYROIDISM

Primary	29 cases
Idiopathic	19
Thyroiditis	5
Iodine 131 ablation	2
Surgical ablation (CA)	1
Congenital	1
Tolbutamide R _x ?	1
Secondary (Sheehan's)	1
Total	30

standard protocol in order to assess changes affecting the cardiovascular, hematopoietic, renal, hepatic and musculoskeletal systems. All laboratory tests were carried out by conventional methods at the Puerto Rico Medical Center Central Laboratory. PBI determinations were performed at a commercial laboratory (Biochemical Procedures, California).

As one of the principal aims of this study was to assess how well would laboratory parameters conform to the clinical appraisal of thyroid replacement, one of the authors would see the patient on each visit and decide dose adjustments without the aid of laboratory data, using common criteria for euthyroidism as shown in Table IV.

In most instances the dates between collection of such samples and the subsequent clinic visit were too close so that results were not available at that particular visit. The protocol's timetable called for 1-2 months visit interval and a minimum treatment period of 6 months. In 11 patients a comparison of PBI levels on Euthroid vs. sodium levothyroxine therapy was carried out.

As is customary, in patients with moderate to severe hypothyroidism small amounts of the medication were started and the dose built up gradually until it was judged adequate. Such selection was facilitated by the availability of various strengths in the following combinations and colors of T4 to T3 (in ug): 180/45 (gray); 120/30 (violet) 60/15 (beige) and 30/7.5 (orange). Patients already receiving thyroid replacement therapy were switched to intermediate doses, adjusted if needed to clinical euthyroidism.

TABLE IV: CRITERIA FOR EUTHYROIDISM

I: From History: Absence or disappearance of:

1. weakness
2. weight gain or edema
3. cold intolerance
4. constipation
5. memory impairment
6. dry skin
7. deafness
8. menstrual problems

II. From Physical Examination: Absence or disappearance of:

1. weight gain
2. puffiness of face
3. peripheral edema
4. coarse hair / scarce eyebrows
5. paleness / yellowishness
6. coarse, dry skin
7. cold skin
8. slow pulse
9. cardiomegaly
10. pendular DTR's

III. From diagnostic aids:

1. PA chest film (heart size)
2. EKG (voltage, rate, ST - T wave changes).

Results

The most frequent presenting symptoms were tiredness, weakness, cold intolerance, loss of appetite, constipation, memory impairment and weight gain. The physical findings, as in the case of symptoms, were most noticeable among those presenting moderate to severe hypothyroidism. Skin pallor, slow speech and characteristic facies were present in all severe and moderately severe cases. Pulse rate varied from 56 to 96 beats per minute at rest with a mean of 70.1 beats per minute. In 15 patients, there was a significant rise in pulse, averaging 19 beats/min., as the patient went from the hypothyroid to the euthyroid state, from 69 to 88 beats/min. Blood pressure and pulse among the rest of the patients had variable responses. Facial edema, puffiness, leg edema and body weight were clearly referable to the presence of excess fluid. Indeed, all but 4 patients lost weight upon therapy, its extent correlating with severity of the disease: mean weight losses were: -4.75, -8.5 and -14.3 lbs. among the mild, moderate and severely hypothyroid groups respectively (Fig. 1).

Neurological changes, other than improved cerebral function, were limited to the deep tendon reflexes, which correlated well with severity of the disease. A markedly delayed recovery phase was observed in 19 patients and a mild delay in another 7. Other than

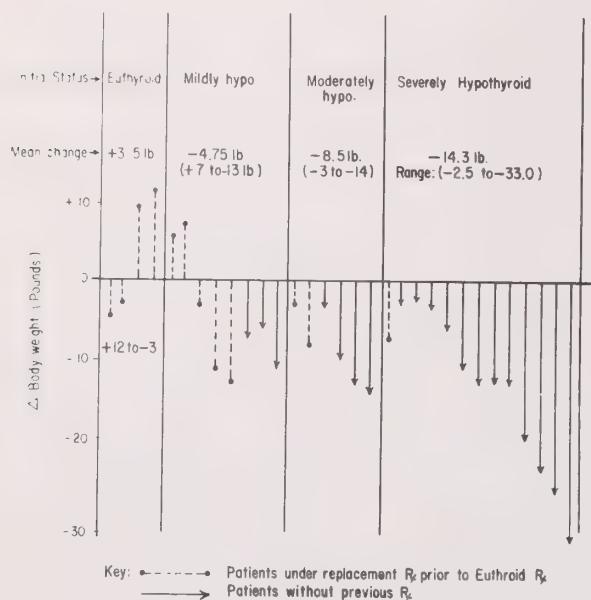
TABLE V: PATIENTS WITH ABNORMAL TRANSAMINASES

Case	Patient	Age	Sex	↑ Heart	↑ Liver	Wt.loss *	SGOT/SGPT **		
							Baseline	1 mo R _x	2-8 mo R _x
2	ERA	42	F	+	+	17 lbs.	72/68	130/82	102/106
6	VSP	50	M	-	-	5 lbs.	95/46	25/31	31/37
18	AVS	34	F	+	-	18 lbs.	80/160	21/31	50/45
21	LMG	35	M	+	+	33 lbs.	134/120	60/145	50/126-64
29	CCC	50	F	+	-	19 lbs.	60/30	27/46	112/116-22/25
30	DRO	29	M	-	-	13 lbs.	71/60	22/44	29/38
Averages		40				17.5	85/81	48/64	47/53

* - Total change from hypo to euthyroid state

** - Normal values: SGOT: 12-40 units; SGPT: 10-45 units

Fig.1 EFFECT OF "EUTHROID" THERAPY ON BODY WEIGHT -By Severity



weight loss and disappearance of edema, improvement in the recovery phase of the deep tendon reflexes was one of the early objective criteria of improvement, usually within 1-4 months.

Cardiomegaly, as judged either by physical examination or X-rays or both, was seen among 7 patients, whose mean age was 47.6 years (range: 34- 62). In two of these, the cardiomegaly persisted after the treatment. They were known to have underlying arteriosclerotic heart disease and diabetes. One of these patients was euthyroid at the time of switching her to Euthroid. The other 5 patients were all severely hypothyroid. The cardiac size became normal in 1 to 4 months, accompanied by a weight loss ranging from 11 to 33 lbs. at the time of becoming euthyroid.

Electrocardiographic changes were observed frequently among the moderate to severely hypothyroid patients: 21 had one or more of the following findings: low voltage, flat T waves and inverted T waves. All ECG's reverted to normal except in a patient with left ventricular hypertrophy and hypertension.

Laboratory Findings

Laboratory data comprising hemograms, urinalyses and blood urea nitrogen did not show any appreciable alterations. The two hour post-prandial blood sugar was abnormal in 4 instances. In one, a diabetic oral

glucose tolerance test (GTT), was confirmed, while in the other 3, an abnormal but not definitely diabetic GTT was found. A patient had pre-existing diabetes mellitus.

The liver profile included: serum transaminases (SGOT, SGPT), thymol turbidity, alkaline phosphatase, serum albumin and globulin. In 6 patients, abnormal SGOT were obtained (Table V).

Four had SGPT elevations prior to therapy, while in 2 elevations occurred at 2-4 months of treatment. These enzymes returned to normal values within 2-6 months, and were not accompanied by other data that would point to parenchymal hepatic or cardiac damage, except for patient LMG, in whom thymol turbidity and BSP were abnormal. A patient with variable elevations of serum alkaline phosphatase and aggravation of unilateral gynecomastia upon therapy was extensively studied, but final confirmation of liver disease by means of liver biopsy was not possible.

Average serum cholesterol levels among previously treated patients was 192mg/100ml. Among the untreated group, the mean value was 270mg/100ml. At the end of 4 -6 months all patients had normal serum cholesterol levels (mean : 164mg/100ml.), ranging from 75 to 230mg. Among the different groups, the time required to achieve euthyroidism varied from 1 - 8 months irrespective of severity, and averaged about 3 months for all groups.

The average serum PBI among those previously treated was 5.3 ugm/100ml., while among the untreated, it was 2.9 ugm/100ml. At the end of Euthroid therapy, the mean PBI for the whole group was 5.2 ugm/100ml. (Table VII). PBI values under 4 ugm/100ml., were obtained in only 2 instances (3.2 and 3.4 ugm/100ml.) Fig. 2 shows the correlation between serum cholesterol and PBI. Pre-Euthroid therapy, among 17 patients with PBI less than 4 ugm/100ml., 7 had serum cholesterol above 250mg/100ml., the other 10 being within normal. At the end of Euthroid therapy, 24 out of 25 patients depicted had both normal PBI and cholesterol levels, six having serum cholesterol levels even lower than 150mg/100ml.

All patients responded to exogenous therapy in a predictable fashion. There were two patients, however, who had showed resistance to usual doses of sodium levo-thyroxine, requiring as much as 0.8 mg daily. They could be maintained well on a dose of 240/60ugm of T₄/T₃, roughly equivalent to 4 grains of thyroid extract. As seen in Table IX, 93 percent of all patients could be well replaced and maintained euthyroid on a dose of Euthroid roughly equivalent to 2-3 gr thyroid

TABLE VI: SERUM PROTEINS IN PATIENTS WITH ABNORMAL TRANSAMINASES

Case	Patient	B A S E L I N E				6 M O N T H S R/			
		TP	Alb.	Glob.	A/G	TP	Alb.	Glob.	A/G
2	ERA	7.7	5.0	2.7	1.85	6.1	3.8	2.3	1.65
6	VSP	7.2	5.0	2.2	2.77	6.6	4.0	2.6	1.58
18	AVS	8.3	4.8	3.5	1.37	7.1	4.5	2.6	1.73
21	LMG	7.6	5.4	2.2	2.55	7.8	5.4	2.4	2.25
29	CCC	7.0	4.6	2.4	1.91	7.2	3.6	3.6	1.00
30	DRO	7.2	4.5	2.7	1.67	6.4	4.2	2.2	1.91
Averages		7.6	4.9	2.7	1.84	6.9	4.3	2.6	1.66

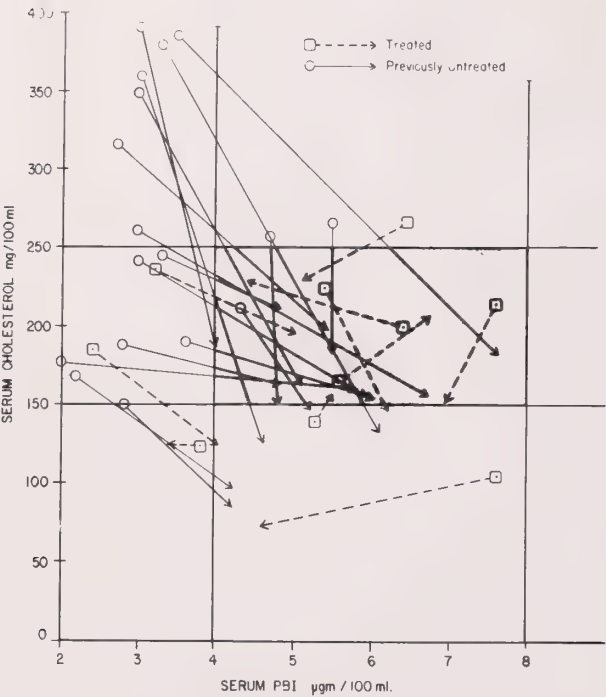
TABLE VII: PLASMA PBI VALUES IN RELATION TO THERAPY

	Treated		No Treatment		Total	After Euthyroid R _x (All pts. euthyroid) x Ave. PBI (Range)
	No. Pts.	Ave. PBI (Range)	No. Pts.	Ave. PBI (Range)		
Euthyroid	4	6.9 (5.4-7.6)			4	5.1 (4.6-6.2)
Mildly hypothyroid	5	4.8 (3.2-6.4)	3	3.3 (3.0-3.6)	8	5.1 (3.4-6.4)
Moderately hypo	2	5.6 (4.7-6.4)	4	2.8 (2.2-3.0)	6	5.3 (4.6-5.8)
Severely hypothyroid	1	2.2	11	2.8 (2.2-3.3)	12	4.9 (3.2-7.5)
Totals	12	5.3	18	2.9	30	5.2

TABLE VIII: DOSE OF "EUTHROID" NEEDED TO MAINTAIN OR ACHIEVE
 A EUTHYROID STATE

Number of Patients	Percentage of Total	Euthroid Dose T ₄ /T ₃ (ugm)	Rough equiv. as Thyroid Extract (Gr.)
2	6.7	240/60	4
7	23.3	180/45	3
2	6.7	150/37.5	2-1/2
19	63.3	120/30	2
Total- 30	100.0		

Fig.2. CORRELATION BETWEEN SERUM CHOLESTEROL AND PBI PRIOR TO AND AFTER EUTHROID THERAPY



extract.

A group of 8 patients, upon completion of their scheduled 6 months therapy with Euthroid, were switched to levo-thyroxine in equivalent doses. PBI's were obtained prior and 2 months after such therapy. Results are depicted in Table X. From an average PBI of 6 μgm percent while on Euthroid, there was a rise of 2 μgm percent, to a value of 8 μgm percent while on levo-thyroxine. Two of the values were clearly above the normal range, at 9.0 μgm percent. In none were concomittant clinical parameters and cholesterol levels suggestive of a higher metabolic rate. In retrospect, 3 patients who had been on T4 therapy prior to Euthroid therapy had serum PBI's that were in average 1.3 μgm percent higher on T4 than while on Euthroid. Thus, it appears that, at equivalent doses of thyroid replacement therapy, T4 yields PBI values that are 1.1 to 3.1 μgm percent higher than while on this combination of T4/T3.

Tolerance to the medication was uniformly excellent, except in SBO, a 70-year old male with diabetes mellitus who had been treated with tolbutamide for the previous 8 years. (See Appendix).

TABLE IX: SERUM PBI AS AFFECTED BY LEVO-THYROXINE & EUTHROID THERAPY

Patient	Euthroid R _x		Levo-Thyroxine R _x		Δ PBI (T ₄ -Euthroid)
	Dose	PBI *	Dose	PBI	
OCD	120/30 μgm	7.6 μgm percent	0.3 mg	9.0 μgm percent	1.4 μgm
CPF	120/30	5.1	0.3	7.1	2.0
ARO	120/30	6.1	0.3	9.2	3.1
MOD	120/30	5.0	0.3	7.0	2.0
JLT	240/60	6.7	0.3	7.8	1.1
RRR	120/30	5.4	0.3	7.7	2.3
Averages:		6.0 μgm percent		8.0 μgm percent	+ 2.0 μgm percent

* Normal: 4-8 μgm percent

TABLE X: AVAILABLE PREPARATIONS FOR THYROID REPLACEMENT

Generic name	Equivalent Dose	Trademarks
Thyroid Extract USP	1 Gr.	T. E. (Armour) Parloid (Lanpar) Thromoloid (Mills) Thyrar (Armour)
Thyroglobulin	1 Gr.	Proloid (Warner-Chilcott)
Sodium levo-thyroxine	0.1 mg	Synthroid (Flint) Letter (Armour) Levoid (Nutr. Control)
Sodium levo-T ₃	25 ugm	Cytomel (SKF)
* Liotrix (Levo-T ₄ /T ₃)	60/15 ugm	Euthroid (Warner-Chilcott) Thyrolar (Armour)

* - Since 1969

Comments

I. Comments on some problems hypothyroid patients may present with

1. Cardiovascular findings:

Cardiomegaly was present in 7 out of 30 patients in this series, and seemed to correlate with severity of the disease. In only 2 was this irreversible (associated with atherosclerosis and diabetes), while in the remaining 5, there was complete reversal of the cardiomegaly. ECG changes were uniformly observed. These were non-specific but very valuable in the follow-up of the patient's course. *Heart failure* was not present in any, even though it was considered briefly in patient LMG. In contrast to cardiomegaly associated with other disease states, that seen in hypothyroidism is usually not accompanied by heart failure nor by chest pains. Some investigators advocate a Valsalva maneuver to distinguish a failing heart from the simply enlarged heart of myxedema (10), but this is usually not necessary except when pericardial effusion is present, as could indeed occur in severe myxedema. The salutary response of cardiomegaly to thyroid replacement therapy alone furnishes the final proof.

The usual slow pulse correlated well with severity of the disease. It is now appreciated that thyroid hormones per se have a positive inotropic and chronotropic effect on the heart and that their apparent potentiating effect on catecholamines seem to be due to a faster metabolic rate leading to a higher content of free catecholamines made available to the myocardium (11,

12).

The previously suggested myocardial activation of cyclic AMP by thyroid hormones does not seem to hold true as the cAMP content of hyperthyroid rat myocardium does not differ from that of control animals (13).

2. Liver function:

Liver function tests are said to be normal in hypothyroidism (14). In the present series, there were 6 patients who had elevations of transaminases (Table V). Abnormalities in liver function tests have been described (15) but they are reversible upon adequate thyroid replacement. In only one patient (Case 21, LMG), was there evidence of liver dysfunction as measured by a BSP excretion of 31 percent. Such elevated transaminases persisted after therapy in 2, both of whom had hepatomegaly initially. (Case 2 and 21). Care must be exercised in ascribing enzyme elevations to hepatic dysfunction, as these could be associated with muscle involvement by hypothyroidism, although it is only rarely that this achieves clinical significance, especially in children, and in myopathy associated with reduced muscle alpha glucosidase (acid maltase) (16).

Contrary to other common causes of liver impairment that may be associated with fluid retention, the liver profile of hypothyroid patients without other underlying problems show a normal or high serum albumin and normal A/G ratios. Our patients (Table VI) had an average total serum protein of 7.6 gm,

(albumin 4.9, globulin 2.7) and their post-therapy values remained normal.

Histologically, Klion et al (17) found hepatic single cell necrosis by light microscopy in 2 patients with myxedema, in whom electron microscopy, revealed slight changes in the smooth membranes of the mitochondria. Both patients, however, had normal liver function tests so far as tested. By contrast, 7 hyperthyroid patients (also with normal liver functions tests), showed non-specific reactive hepatitis by light microscopy, with necrotic hepatocytes and scattered accumulations of macrophages and lymphocytes around them, as well as moderate steatosis and decreased glycogen.

Electron microscope of these biopsies showed changes in the hepatocytic organelles, the most prominent ones being bizarre and enlarged mitochondria and irregularity of the mitochondrial outer membranes. More studies like this one are needed for further elucidation of the liver abnormalities that may be present in thyroid disease states.

3. Fluid retention and edema:

As seen in Figure 1, there was a close correlation between indirect evidence of fluid retention (weight loss upon therapy), and severity of hypothyroidism. Twenty six out of 30 patients (86.7 percent) lost weight upon replacement therapy, mean losses varying from 4.75 in the mild to 14.3 lbs. among severely hypothyroid patients. Such fluid retention may at times mimic a nephrotic syndrome, congestive failure, hepatic cirrhosis and, as in case 10, (FAF), acromegaly. The latter was a 52-year old colored male with a husky physique, big, thick hands and chronic bronchial asthma, who was subsequently shown not to have hypersomatotropinism. His physique improved considerably once his fluid retention disappeared with therapy.

Various mechanisms have been suggested for the fluid retention of hypothyroidism especially seen in myxedema. The most plausible explanation seems to be related to alterations in renal hemodynamics and secretion of antidiuretic hormone. A functional impairment in cardiac output could result in a decreased glomerular filtration rate which could play a role in the tendency for delayed water diuresis, but this seems insufficient to explain the dramatic cases resembling the syndrome of inappropriate ADH secretion. Indeed, myxedema patients given water loads are able to dilute their urine (19), contrary to IADHS. Nevertheless, they seem to need much lower serum osmolalities than a normal would, pointing therefore to a defect in their hypothalamic "osmostat" (18). This could explain why these hypothyroid patients may respond like hypo-

pituitary patients with a correction of their delayed water diuresis by glucocorticoids (19), as glucocorticoids are known to correct such derangement in the hypothalamic "osmostat", lowering its threshold (20).

4. Gynecomastia:

The occurrence of gynecomastia in hyperthyroidism is well recognized (21). Puerperal (22) as well as non-puerperal galactorrhea in female hypothyroids has been described (23). The presence of gynecomastia in hypothyroidism however, seems much less common. Even more unexpected is the finding of apparent aggravation of pre-existing gynecomastia in one of our patients (Case 22, JSN, a 29-year old colored male with hypothyroidism of 9 years duration, probably a case of Hashimoto's thyroiditis). His right breast had glandular tissue measuring 3 x 3 cm. while untreated, and this progressed to 7 x 8 cm. upon therapy, again regressing to 4 x 4cm. three months off therapy. Extensive studies including liver function tests, testicular and breast biopsies, complete adrenal-gonadal steroid tests and pituitary function tests were unrevealing. Similarly unrewarding findings have been reported among patients with hyperthyroidism with gynecomastia (21).

5. Tolbutamide and hypothyroidism:

Case 23, SBO (See Appendix), was hypothyroid clinically and laboratory-wise when seen 8 years after treatment with tolbutamide for diabetes mellitus. The possibility that his hypothyroidism could be due to such therapy, was raised based on the report of Hunton (24), and reinforced by the apparent reversal of symptoms after tolbutamide had been withdrawn and the patient had been off thyroid therapy for several months. At a later evaluation, however, hypothyroidism was again confirmed. This is in keeping with the negative findings of Burke (25) and those of Portioli and Rocchi (26), who found that in spite of a 3 percent abnormal thyroid function tests incidence among sulfonylurea-treated diabetics, no clinical evidence of hypothyroidism were present. Our patient's "transient" improvement would seem to rule out a permanent hypothyroidism on the basis of his previous sulfonylurea therapy.

II. Comments on the relevance of incorporating T3 to thyroid replacement therapy.

The advent of a new therapeutic agent is always welcome if it offers some advantage over established preparations. In the case of Liotrix (Euthroid®), the novelty consists in combining the synthetic forms of tri-iodothyronine and tetraiodothyronine, a combination that was previously only available in England (27). The latter had a T3:T4 ratio for 1:9, which, in the light of recent data, would not appear to be the most physio-

logic proportion (4, 5).

As the human thyroid produces both T3 and T4, it would appear logical to mimic nature's own ways in replacing thyroid extracts. The latter, however, pose problems as to potency (1, 8) and, rarely, may elicit allergic reactions. Synthetic preparation would seem to best assure the purity and accuracy of dosage, with their potency assessed by their calorogenic activity.

It is well known that for the great majority of patients, a synthetic preparation of T4 (listed in Table X) can reverse the symptoms and signs of hypothyroidism in a predictable fashion, and can maintain a euthyroid state. Thus, the metabolic role of T4 has been widely appreciated and even over-estimated. The latter is partly attributable to the relative easiness and inexpensive way in which T4 may be measured indirectly by means of the protein-bound iodine (PBI), by virtue of its strong affinity to thyroxine-binding globulin (TBG). Contrariwise, the metabolic role of T3 had been underestimated until recently, as it took more than 15 years since its identification by Gross and Pitt-Rivers (28) for a suitable means of measuring plasma T3 to appear (29). Since then, and with the advent of radioimmunoassay technique, a better assessment of its role has been possible.

Indeed, on closer analysis, the stronger affinity of T4 for TBG imposes a slower disposal rate and diminished tissue permeability, as compared with T3, so that TBG-bound T4 amounts to a reservoir form of the hormone. Such TBG binding is not essential to hormone action, as normal thyroid function is the rule among patients who are either deficient (30, 31, 32) or over abundant (33) in such inter-alpha globulin.

As had been suspected long ago, the delayed onset of action of administered T4, other than due to considerable binding to TBG, can be attributed to the time required for conversion into T3, mediated by monoiodinases in tissues. Thus, it has been estimated that up to 42 percent of the T3 produced daily (12 out of 29 μg), derives from peripheral conversion from T4 (34), the production of the latter being around 92 μg /day. Such significant peripheral T4 to T3 conversion confirms T4 as a precursor of T3, the latter regarded then as the most metabolically active hormone. This could achieve clinical relevance in the particular patient who is presumably totally or partially deficient in such tissue monoiodinases, and who proves resistant to therapy with T4 alone, as seen in two of the patients in the present series (See Appendix).

Yet, as a rule, either synthetic T4 or T3 can bring about complete reversal of hypothyroidism and myxe-

dema, Thyroxine, however, would normally tend to be absorbed to lesser extent than T3 (35, 36) and even less so in cases of diarrhea, nephrosis or in connection with the ingestion of soybean protein (37).

It has been postulated, that the much faster degradation of T3 and its greater volume of distribution as compared with T4 implies a preferential secretion of T3, especially in view of an intrathyroidial T4:T3 ratio of nearly 4:1 (38). There could arise a situation that would call for such preferential secretion or administration of T3, such as in the treatment of a hypothyroid pregnant woman who has given birth previously to an athyreotic cretin. It has been found that whereas T4 passes the placental barrier slowly and possibly incompletely, T3 seems to pass more readily. However, in order to achieve physiologic levels in the fetus, doses as high as 4 times the usual ones might be required, if tolerated by the mother (39).

Finally, the better absorption and faster action of T3 make it a mandatory component of the therapy in myxedema coma, if a fatal outcome is to be avoided.

III. Comments on the use and abuse of PBI in diagnosis and evaluation of hypothyroidism.

PBI determinations are probably the most widely used tests for assessment of thyroid function. Nevertheless, it is well known that this test has serious limitations imposed by the amount of TBG present in any given plasma. The list of instances where such changes in TBG plague the results of the PBI is impressive. Most frequently, TBG is elevated by estrogen therapy or pregnancy, yielding spuriously high PBI's, or decreased by drugs like phenylhydantoin, androgens, salicylates, and many others. Tests like the triiodothyronine-resin uptake, which give an indirect assessment of TBG, or actual measurement of TBG may clarify matters further, but the fact remains that all laboratory tests must subordinate to the overall clinical assessment of the patient, which stands as the most reliable means. It is to be expected that direct measurement of free T4 and free T3 by radioimmunoassay and competitive protein binding techniques will render PBI and similar tests obsolete, but in the meantime, PBI's shall continue being used diagnostically and sadly abused in the assessment of adequacy of replacement therapy. Under present circumstances, therefore, a combination-type preparation correlating as closely as possible with the true state of affairs

in the patient would seem preferable. It is well known that therapy with T4 alone yield higher than expected values for PBI, as shown in the present series among 9 patients in whom this was investigated (Table X). In

two of these patients PBI values while on T4 therapy were definitely above the normal range, yet the patients were clinically euthyroid. Such higher than expected PBI's can be explained on the basis of the higher TBG binding of T4. The opposite finding, a lower than expected value during therapy with T3 is not so readily understood.

T3 leads to an accelerated disposal rate of T4 by virtue of an enhanced metabolic rate. This is suggested by studies which have shown that T3 lowering of plasma PBI cannot be explained on the basis of suppression of endogenous T4 among euthyroid subjects, for the same PBI lowering effect by T3 therapy is observed among hypothyroid patients under constant therapy with T4 (40).

Again, clinical judgment must remain on top of our diagnostic tools, for even the advent of such sophisticated laboratory tests, as free T3 and free T4 radioimmunoassays cannot completely avoid some overlapping between the normal range of values and those of hypothyroid patients (41). However, in the early detection of hypothyroidism, measurement of TSH levels may prove to be a useful tool (42).

Summary

The efficacy of Euthroid ®, (a combination of thyroxine (T4) and triiodothyronine (T3) in a 4:1 ratio), on the induction or maintenance of a euthyroid state, was studied in a group of 30 hypothyroid patients, all but one of primary etiology. There were 20 females and 10 males with an age range 15-70 years. Eighteen (18) were previously untreated, while 12 were being treated. Only 4 were considered euthyroid at the onset of Euthroid ® treatment, while severity of hypothyroidism on clinical basis was: severe in 12, moderately severe in 6, mild in 8.

A euthyroid state was achieved among the latter group within 1-8 months, with an average of 3 months, irrespective of initial severity. The dose most frequently rendering and (or) keeping the patient euthyroid was that containing 120ug T4 and 30ug T3, and which appeared roughly equivalent to 0.3 mg levo-thyroxine (l-T4). Two patients who were unresponsive to usual doses of l-T4 responded well to Euthroid. There was generally good agreement between clinical status and PBI plasma levels. In 6 patients in whom the comparison was made, average PBI levels were 2 ugm percent higher (8.0) while on l-T4 treatment than while on Euthroid ® (6.0 ugm percent).

The new preparation appears well tolerated and

seems to be a useful addition for replacement treatment in hypothyroidism.

The important physiologic role of T3 is emphasized and some special clinical problems are discussed in the light of newer knowledge on pathophysiological mechanisms in hypothyroidism.

Resumen

Se informa la experiencia del manejo clínico de 30 pacientes con hipotiroidismo con una nueva preparación de hormonas tiroideas: Euthroid ®, la cual es una combinación de tiroxina (T4) y triyodotironina (T3), sintéticas, en proporción de 4:1 respectivamente.

La edad de este grupo de pacientes era de 15 a 70 años; 20 eran mujeres y 10 varones. Dieciocho no habían sido tratados previamente, mientras que 12 estaban ya en terapia de reemplazo. El grado de hipotiroidismo inicialmente era: severo en 12, moderado en 6, y leve en 8 pacientes. Sólo cuatro estaban eutiroides al comienzo de la terapia con Euthroid ®.

Se logró eutiroidismo en todos los pacientes en 1 a 8 meses, y en 3 meses como medida promedio; irrespectivo de la severidad inicial del hipotiroidismo.

La dosis con la cual se logró inducir y mantener un estado de eutiroidismo más frecuentemente correspondió a la combinación de 120 ugm T4 y 30 ugm T3 ("Euthroid 2"), que parece ser aproximadamente equivalente a 0.3 mg de levo-tiroxina. Dos pacientes que no respondían a dosis usuales de tiroxina (T4), respondieron bien a Euthroid ®.

Se observó una buena correlación entre la evaluación clínica y los niveles del yodo protéico plasmático (PBI). En 6 pacientes, el nivel promedio del "PBI" fue mayor durante tratamiento con tiroxina (8.0 ugm por ciento) que durante la terapia con Euthroid ® (6.0 ugm por ciento).

La nueva preparación parece ser bien tolerada y útil en la terapia de reemplazo para hipotiroidismo.

Se enfatiza el importante papel fisiológico de la triyodotironina (T3), y se discuten algunos problemas clínicos especiales del hipotiroidismo a la luz de conocimientos recientes sobre mecanismos fisiopatológicos de esta condición.

Appendix

Selected Case Reports

Case 23. SBO UDH No. 03-58-71

A 70-year old white male had been found to have diabetes

mellitus 8 years prior to his visit to our General Medicine Clinic. He had been treated with tolbutamide, 1-2gm. daily, without adequate control of his hyperglycemia. He complained of epigastric burning sensation and fullness, which had prompted performing upper gastrointestinal series on two occasions, with negative results. He also had constipation, cold intolerance and memory impairment.

On physical examination he was a well developed, well nourished, lethargic-looking male. B.P. 120/80, P. 60 regular. He had a sad facial expression and mild puffiness. There was loss of lateral eyebrow hair. Fundoscopic examination revealed few microaneurysms and increased light reflex of the arterioles. The thyroid gland was palpable but not enlarged. It was firm, not tender nor nodular. Heart sounds were distant but there was no cardiomegaly. Neurological examination was negative except for mild delay in the recovery phase of the deep tendon reflexes.

Hypothyroidism was suspected. A 24 hr. iodine 131 uptake was 6.6 percent, PBI 3.5 ugm percent, serum cholesterol 180mg percent; normal hemogram, BUN and liver function tests were found. ECG showed left ventricular hypertrophy by voltage, flattening of T waves in standard limb lead and V4-V6. His diabetes was in poor control: morning blood sugars ranged from 200 to 350mg percent. Urinalysis showed traces of albumin.

Insulin therapy was refused by the patient when tolbutamide was discontinued, so DBI-TD was started at 50mg b.i.d. Euthroid 30/7.5 ugm. (T4/T3) was given during 2 weeks, then increased to 60/15 for another 2 weeks. At this time cold intolerance and constipation were partially relieved. Physical examination was unchanged. PBI was 5.0 ugm percent.

About one month later he discontinued Euthroid because of "fever", bloating, and epigastric discomfort, which he attributed to the medication. Phenformin was discontinued and insulin was again suggested, but refused by the patient, who was then started on Diabinese, 250mg b.i.d. This failed to bring his diabetes under control. A month later he was seen complaining of numbness of both legs and feet. Vibration sense was intact bilaterally. Deep tendon reflexes were within normal. Insulin therapy was finally accepted, and started at 15 units NPH daily. Vitamin B-12 was also given parenterally. He was doing better within a month. He appeared euthyroid. PBI was 4.2 ugm percent.

Subsequently the patient required up to 60 units NPH insulin for control of diabetes and appeared euthyroid for several months, without cold intolerance, constipation or significant memory impairment. However, at the end of 2 years of observation, he again appeared hypothyroid, with a sallow complexion and with some of his old symptoms. The 24 hr. iodine uptake was 4.6 percent and PBI was 2.4 ugm percent. Thyroid replacement therapy was then restarted and maintained.

Case 6 VSP UDH No. 03-64-28

A 50-year old white male had documented hypothyroidism for 17 years. He was admitted to our study in May 1967. His disease had proved resistant to levo-thyroxine (T4) in spite of daily doses up to 0.8mg. During the previous year he had had partial alleviation of his usual symptoms while on triiodothyronine (Cytomel ®), 125 ugm daily. During one month prior to our evaluation the patient had been off therapy. He appeared obviously hypothyroid, and complained of weakness, lethargy, cold intolerance, poor appetite and mild memory impairment.

B.P. 94/70, P. 68, Weight 123 lbs. He had coarse skin, thick eyelids and yellowish complexion. He had slow speech. Deep tendon reflexes were pendular; the rest of his physical examination was unremarkable. Serum cholesterol was 184 mg percent, PBI 2.2 ugm percent. CBC, urinalysis, BUN, 2 hr. post prandial blood sugar, thymol turbidity, total serum proteins and A/G ratio, were all within normal limits. SGOT was 95 units, SGPT 46 units. Chest film was normal. ECG showed low voltage, with flattened or inverted T waves in most leads.

After one month therapy with Euthroid 120/60, he lost 7 lbs. and looked much less hypothyroid. DTR's were still pendular. Serum cholesterol had dropped to 86mg percent, while PBI rose to 5.3 ugm percent. SGOT was 25 units, SGPT 31 units, and there was reversion of previously inverted T waves in the ECG.

Euthroid was eventually raised to 240/60, and after 4 months of therapy he was clinically euthyroid. Serum cholesterol was 136mg percent, PBI 3.7 ugm percent, and all other laboratory studies and ECG were normal.

The patient continued doing well for the next 4 months, but was then seen by a physician unaware of his special therapeutic regime with Euthroid, and prescribed 0.5mg levo-thyroxine instead. When seen 4 months later, and while still on such therapy, he was having characteristic symptoms and signs of hypothyroidism. He had gained 12 lbs., was puffy, pale and had a slow speech. BP. 100/70, P. 64, DTR's were pendular. Serum cholesterol was 148 mg percent, PBI 2.7 ugm percent. Routine laboratory studies were within normal, but SGPT was 500 units and SGOT 60 units. Total protein was 7.4 gm percent, albumin 4.6 and globulin 2.8. There were again non-specific T waves changes in the ECG. There were no cardiovascular symptoms. He was then given 75 ugm Cytomel and 0.2 mg Synthroid with fairly good results, and was later switched to his usual replacement with Euthroid.

Case 13 IAM UDH No. 02-93-16

A 49-year old non-white male, had had symptoms of hypothyroidism since 6 years prior to his admission to the study. He had not responded well to 0.3 mg Synthroid, which he took from 1963 to 1965. During the following 2 years he had his dose of T4 raised to 0.5 mg daily, which he was taking when first seen by us. He presented with moderate weakness, tiredness, cold intolerance and memory impairment. BP 100/70, P 72. He appeared pale and mildly puffy, had a coarse, cold skin, a slow speech and pendular deep tendon reflexes. Serum cholesterol was 140 mg percent, PBI 5.3 ugm percent. All other pertinent laboratory tests, PA chest film and ECG were within normal.

During the next 6 months, while on Euthroid, 180/45 ugm, he showed clinical improvement. There was an initial 5 lbs. weight loss at the end of one month of therapy. PBI's and cholesterol remained normal throughout.

After 8 months of therapy he had regained 12 lbs. of body weight, felt somewhat tired and looked mildly hypothyroid. The skin was moderately coarse and DTR's were somewhat pendular. He denied departure from therapeutic regime. All laboratory data were normal. Euthroid was raised to 240/60. After 2 months, he was again feeling well, had resumed work, had lost 7 lbs. and his DTR's were normal. Serum cholesterol was 121mg percent, PBI 6.5 ugm percent. He has continued doing well.

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RESISTENCIA PRIMARIA A DROGAS ANTITUBERCULOSAS EN PUERTO RICO

De un grupo de 10 enfermos con tuberculosis pulmonar, que nunca antes habían recibido quimioterapia antituberculosa, 8 albergaron bacilos de tuberculosis resistentes a 2 o más drogas antituberculosas. Este hallazgo, informado por los doctores Figueroa y Zack, es motivo de serias preocupaciones en cuanto al origen de tan alta incidencia de resistencia primaria a drogas antituberculosas. Los resultados de los exámenes bacteriológicos de esputo en esos pacientes son altamente confiables, ya que provienen de un laboratorio de competencia incuestionable.

La población de enfermos de este informe está limitada exclusivamente a veteranos y la muestra es muy pequeña. Podemos decir que la muestra no es representativa de la población total de los enfermos de tuberculosis en Puerto Rico. Además la incidencia de resistencia primaria a drogas antituberculosas es de menor importancia como factor en la producción de fallas en los resultados de quimioterapia, según se demostró en el estudio de Hong Kong, informado en la vigésimoprimera Conferencia Internacional de Tuberculosis celebrada en Moscú en julio de 1971. Del estudio de Hong Kong se desprende que si se da quimioterapia inicial con 3 drogas y se hace caso omiso de los resultados de resistencia a drogas, se generan fallas de quimioterapia en solamente un 5 por ciento de los enfermos (en poblaciones de enfermos que tengan incidencia de resistencia primaria de 30 por ciento).

A pesar de lo dicho en el párrafo anterior, nos preocupa grandemente, otra implicación de esta situación. Las más probables fuentes de infección de los enfermos que no han recibido quimioterapia antituberculosa y cuyo esputo tiene bacilos de tuberculosis resistentes a drogas antituberculosas son pacientes cuya tuberculosis ha sido tratada inadecuadamente, bien sea por parte del médico o por falta de cooperación del paciente. Ambas dificultades pueden remediarse mediante programas educativos para médicos sobre el manejo de la tuberculosis y mediante esfuerzos para seguimiento de los enfermos para asegurar que no hay interrupciones en la quimioterapia antituberculosa.

La Asociación Puertorriqueña Antituberculosa y de Salud Respiratoria está celebrando una serie de cursillos para médicos sobre el tema del tratamiento moderno de la tuberculosis. Es de vital importancia diseminar conocimientos sobre la tuberculosis especialmente ahora que la tuberculosis se trata más y más en hospitales generales. Con la cooperación del Departamento de Salud se puede hacer una campaña educativa intensa para médicos, enfermeras, técnicos de Salud Pública, trabajadores sociales, y educadores en salud. Esto aplica especialmente a todo el personal médico y paramédico del Departamento de Salud, ya que la tuberculosis se trata principalmente bajo los auspicios de esa agencia.

Idealmente, deben hacerse estudios de sensibilidad a drogas en todos los enfermos de tuberculosis para control adecuado de la quimioterapia y como guía adicional a la observación clínica, radiológica y bacteriológica. Aceptando la realidad de las facilidades disponibles en nuestra isla, sugerimos las siguientes medidas en Puerto Rico:

1. Iniciar quimioterapia antituberculosa con 3 drogas primarias (estreptomycin, isoniácida y etambutol) por 3 a 6 meses y de ahí en adelante 2 drogas (isoniácida y etambutol) hasta un total de 2 o 12 años.

2. Administrar las dosis totales del día de isoniácida y ethambutol en una sola dosis por la mañana para disminuir la omisión de dosis de una u otra droga durante el día.

3. Seguimiento intensivo por enfermeras y técnicos de salud pública para asegurar que el paciente sigue fielmente su tratamiento sin interrupciones.

4. Cultivos de esputo para bacilo de tuberculosis cada 2 meses como mínimo, sin estudios de resistencia a drogas específicas. Añadir otra droga primaria o secundaria al régimen, sin discontinuar las otras, si hay persistencia de esputo positivo.

Siguiendo tal programa podemos esperar éxito en más de 90 por ciento de los enfermos bajo quimioterapia antituberculosa. La tuberculosis es la más curable de las enfermedades clínicas y puede erradicarse. Hagamos todos un esfuerzo porque así sea en Puerto Rico.

Edmundo R. Figueras, MD
Presidente,
Asociación Puertorriqueña Antituberculosa
y de Salud Respiratoria

RECOMENDACIONES PARA LA MEJOR UTILIZACION DE SANGRE Y SUS COMPONENTES

El "Joint Commission on Accreditation of Hospitals (JCAH) y la Asociación Médica Americana (AMA) recomiendan enérgicamente que la facultad médica de todo hospital activamente regule y supervise la utilización de sangre (1, 2). La organización y la labor que debe llevar a cabo el comité de transfusiones en todo hospital han sido resumidas en el panfleto que publica la AMA (2). Sin embargo, la labor de dicho comité se dificulta si no existen guías generales para la mejor utilización de sangre (3). El propósito de esta comunicación es someter algunas recomendaciones que pueden ser útiles al respecto:

I. Justificación de una transfusión: Se debe administrar sangre a un paciente solamente cuando existe una indicación clara para la transfusión. El componente (sangre completa, células rojas apiladas, plasma, etc.) debe ser específico para la necesidad clínica del paciente. El record médico debe reflejar claramente la justificación para cada transfusión que reciba un paciente.

II. Recomendaciones generales:

A. Anemia — Anemia de por sí no es una indicación para transfusión si el paciente puede tratarse con éxito por otros medios ya sean médicos o quirúrgicos. Todo paciente con anemia debe ser evaluado para determinar la causa de la misma. La transfusión no es la terapia primaria en la mayoría de los casos de anemia sino, más bien, terapia de soporte a ser instituída solamente cuando existen indicaciones específicas.

B. Anemia aguda — Incluye principalmente aquélla asociada a pérdida de sangre y se justifica la transfusión cuando hay evidencia clínica de hipovolemia, shock, hipoxia, o fallo cardíaco precipitado por la anemia.

C. Anemia crónica — Usualmente no es una indicación para transfusión excepto cuando hay evidencia clínica de hipovolemia, shock, hipoxia, o fallo cardíaco precipitado por la anemia. La única otra indicación en estos casos es para mantener una hemoglobina adecuada en pacientes con fallo medular (anemia aplásica, leucemia, etc.). Debe recordarse que en presencia de fallo cardíaco es recomendable medir la presión venosa central además de usar diuréticos y digital. La transfusión debe hacerse lentamente.

III. Recomendaciones específicas:

A. **Transfusión preoperatoria** — No está indicada cuando la causa de anemia no ha sido establecida excepto en casos de urgencia o emergencia. Tampoco está indicada para llevar la hemoglobina a un nivel arbitrario, particularmente cuando se trata de una anemia crónica a la cual se ha adaptado el paciente.

B. **Hemorragia** — (Operatoria, traumática, gastrointestinal u otra). (Refiérase a II B).

C. **Fallo congestivo** — Transfusión está indicada si el grado de anemia es factor importante en el fallo y interfiere con su control o si hay evidencia de hipoxia. Se debe usar células rojas apiladas exclusivamente.

D. **Cirrosis** — Se justifica transfusión solamente cuando existe una indicación específica como hipoxia, shock o fallo cardíaco precipitado por la anemia. Se debe usar células rojas preferiblemente pero si el paciente está sangrando por deficiencia de factores debe usarse sangre fresca.

E. **Uremia** — El paciente con fallo renal crónico usualmente estabiliza su hemoglobina a niveles de 7 a 9 gm por ciento. Se debe administrar transfusión de células rojas solamente bajo indicaciones específicas.

F. **Hemoglobinopatías** — Usualmente este paciente mantiene niveles de hemoglobina de 8 a 9 gm por ciento a menos que ocurra una crisis hemolítica. La crisis dolorosa en drepanocitosis no es de por sí una indicación para transfusión ya que en la mayoría de los casos se puede tratar de otras maneras. Si las crisis son prolongadas y serias la hipertransfusión puede ser de ayuda y debe usarse solo células rojas.

IV. Contraindicaciones para transfusión:

A. "Como un tónico"

B. "Para proveer proteínas y nutrición".

C. "Para fortalecer las defensas del organismo contra infecciones".

D. "Para proveer hierro".

E. "Profilácticamente por pérdida de sangre potencial".

F. "Profilácticamente porque se anticipa hipotensión".

G. En el tratamiento de hipotensión debido a drogas, anestesia, o shock no asociado a pérdida de sangre o plasma.

H. "Para que el paciente se sienta mejor".

I. Para satisfacer exigencias del paciente, familiares, o médicos de que "se haga algo por el paciente".

J. Como sustituto para otro tratamiento médico o quirúrgico.

La mayor y más grave contraindicación para una transfusión es la ausencia de una indicación.

Antonio J. Grillo-López, MD

Referencias

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TRANSFUSIONES DE SANGRE

En este número del Boletín, el Dr. Antonio Grillo enumera una serie de recomendaciones para la mejor utilización en nuestros hospitales de sangre y sus componentes. Estas recomendaciones son de actualidad.

Tras muchos años de debate el Gobierno norteamericano y la Asociación Americana de Bancos de Sangre (AABB) han establecido como meta inmediata la creación de un sistema de Bancos de Sangre que dependan de donaciones voluntarias. La Cruz Roja Nacional ha defendido este principio desde la fundación de su programa de sangre.

Es un hecho establecido que la incidencia del Antígeno de la hepatitis B y de la hepatitis asociada a transfusiones es mucho mayor cuando la sangre proviene de donantes pagados. A menudo hay necesidad de pagar a éstos debido a la escasez de voluntarios. La nueva meta de usar sangre no pagada obviamente ha de causar escasez de sangre, a menos que haya cambios en este sistema que ha dependido fuertemente en su uso. El primero de estos cambios ha de ser una regulación del uso de sangre en todos nuestros hospitales. De aquí surge la actualidad de las recomendaciones del doctor Grillo. Otras medidas serán necesarias; una es el fortalecimiento de aquellas instituciones dedicadas a obtener sangre donada voluntariamente. Si bien es importante que el Departamento de Salud tome parte activa en esto, es realmente sobre el público donde recae esta responsabilidad. Sobre los médicos recae la responsabilidad de educar a sus pacientes y a los familiares de éstos. Los pacientes deben de conseguir de sus familiares y amigos que donen sangre para ellos antes de cirugía electiva y cuando transfusiones sean necesarias.

La otra medida es de simple aritmética y también recae sobre el médico. La sangre completa sólo tiene una indicación; "shock" o peligro de "shock" debido a hipovolemia. En todos los otros casos no está indicado su uso, y además su uso de sangre completa es antieconómico, ya que se le administra al paciente todos los otros componentes sanguíneos no necesitados por él. El uso de los componentes sanguíneos, y en particular células rojas apiladas permite que una unidad de sangre pueda ser usada para tratar a varios pacientes (Factor 8, Plaqueta, Plasma y sus variaciones). Apoyamos las recomendaciones enumeradas y exhortamos a los médicos que las adopten.

Francisco J. Muñiz, M. D.

CARTAS AL EDITOR

Dr. Jorge O. Just Viera, Editor
Boletín Asociación Médica de Puerto Rico
Santurce, Puerto Rico

Estimado doctor Just Viera:

Origen del Negrete

Al reabrirse el Hospital Universitario de la Escuela de Medicina Tropical en 1940 los sigmoidoscopios que fueron comprados eran de bakelita negra de la casa Cameron. Estos sigmoidoscopios eran utilizados diariamente en el examen de los enfermos bilharzianos y de esprú tropical.

Durante el año 1942 vino a trabajar en el Hospital Universitario un médico Colombiano quien le aplicó el nombre de negrete a la sigmoidoscopia por utilizarse los sigmoidoscopios negros. De ahí en adelante se ha divulgado por todo Puerto Rico así como también fuera de la Isla el apelativo de negrete para la sigmoidoscopia. No tuvo nada que ver el hecho que durante esos años vivía un actor de cine mejicano muy admirado y querido en nuestra Isla.

F. Hernández Morales, MD

Dr. Jorge O. Just Viera, Editor
Boletín Asociación Médica de Puerto Rico
Santurce, Puerto Rico

Distinguido señor Director:

Este breve estudio estadístico, preparado por la Administración de Seguro Social, nos revela el grado de participación que tiene Puerto Rico en el Programa de Determinación de Incapacidad Federal.

En él se comparan las estadísticas de Puerto Rico con las de los Estados Unidos y establece una comparación de las causas más comunes de incapacidad entre Puerto Rico y los Estados Unidos.

Considero interesantísimo y hasta intrigante, la mayor preponderancia de enfermedades mentales, siconeuróticas y de desórdenes de la personalidad en nuestro ambiente al compararlo con el continente. Este dato merece estudio a fondo, e invito a nuestros colegas siquiátras a que se expresen sobre esta situación, única en todo el Programa.

Agradeceré se le dé cabida a este trabajo en uno de los próximos números de nuestro Boletín.

Jaime F. Pou, MD
Director Médico
Programa Determinación Incapacidad

DIAGNOSTIC PATTERNS IN DISABILITY IN PUERTO RICO AND THE NATION

Under the provisions of the social security disability program, the nation's largest disability plan, a worker under 65 can receive monthly benefits if he or she becomes unable to work due to a mental or physical impairment that has lasted —or is expected to last — at least 12 months or is expected to result in death.

More than 96 million workers can count on monthly cash benefits in the event of such severe and extended disability. In addition, the dependents of these workers are also eligible for monthly benefits. Over 1.8 million workers and 1.4 million dependents are now receiving disability benefits at the rate of almost \$5 billion a year.

Currently, 31,368 disabled workers in Puerto Rico are collecting \$4,092,423 a month in benefits. In addition, 11,275 wives or husbands of disabled workers and 45,468 children of disabled workers in Puerto Rico are receiving \$304,627 and \$1,017,709, respectively.

The latest year for which tabulated data is available showing disabled worker diagnostic patterns by State is 1970. Disabled workers in Puerto Rico who began receiving benefits in that year constituted 5,096 of the 350,384 new beneficiaries nationwide.

Table I compares the frequency of diagnostic groups

in Puerto Rico with the U. S. overall. It shows that diseases of the circulatory system comprised the largest diagnostic group in the country in 1970. Diseases of the musculo-skeletal system and mental disorders, including psychoneurotic and personality disorders, were the second and third largest diagnostic groups, respectively. All States do not, however, follow this pattern.

Within these overall diagnostic groups, the most prevalent primary diagnosis in the nation in 1970 was chronic ischemic heart disease. Puerto Rico recorded 474 cases that year. The nation's second most common primary diagnosis and the most prevalent in Puerto Rico, schizophrenic disorders, accounted for 1,007 cases in Puerto Rico. Following these, in order of decreasing national prevalence, was osteoarthritis and allied conditions, with Puerto Rico reporting 204 cases, followed

by emphysema with 79 cases. There were 215 cases of displacement of intervertebral disc in Puerto Rico; 147 cases of diabetes mellitus, and rheumatoid arthritis and allied conditions accounted for 37 cases in Puerto Rico that year. Cerebrovascular disease, listed eighth among the most prevalent primary diagnoses in 1970, recorded 68 cases in Puerto Rico; malignant neoplasm of trachea and lung 22 cases; and neuroses ranked tenth with 278 cases.

Additional information about the social security disability program in Puerto Rico can be obtained through the Puerto Rico State Agency of the Disability Determination Program, 1503 Asia St., Santurce, Puerto Rico or by telephoning Dr. Jaime F. Pou, Chief Medical Consultant, at 724-8938.

TABLE I: SOCIAL SECURITY WORKER DISABILITY ALLOWANCES 1970 — DIAGNOSTIC GROUPS

Diagnostic Group		U. S.	Puerto Rico	
Diseases of the circulatory system	108,906	31.1 percent	880	17.3 percent
Diseases of the musculo-skeletal system	52,086	14.9 percent	703	13.7 percent
Mental, psychoneurotic, and personality disorders	38,406	11.0 percent	1,738	34.1 percent
Neoplasms	36,095	10.3 percent	294	5.8 percent
Accidents, poisonings, and violence	28,231	8.1 percent	342	6.7 percent
Diseases of the respiratory system	24,254	6.9 percent	200	3.9 percent
Diseases of the nervous system and sense organs	22,575	6.4 percent	369	7.2 percent
Allergic, endocrine system, metabolic, and nutritional diseases	13,141	3.8 percent	185	3.6 percent
Diseases of the digestive system	9,051	2.6 percent	110	2.2 percent
Infective and parasitic diseases	8,760	2.5 percent	112	2.2 percent
Other	8,875	2.5 percent	163	3.1 percent
Total -	350,384	100.0 percent	5,096	100.0 percent

* - Figures may not total 100.0 due to rounding.

NOTICIAS

FROM AMA NEWS:

WINE AND BEER BENEFIT MANY ELDERLY PATIENTS

CHICAGO — Wine and beer in moderation is good for the physical and emotional ills of elderly patients, says an editorial in the Nov. 12th issue of the *Journal of the American Medical Association*.

Thomas B. Turner, M. D., of The Johns Hopkins University School of Medicine, Baltimore, cites in the editorial a number of studies showing beneficial effects of a bottle of beer or a glass of wine among patients in nursing home situations.

The therapeutic effect of mild alcoholic drinks is considerably enhanced if the beverages are given in a pleasant group situation, Dr. Turner says. In one study the patients had their drinks in a room equipped like a pub, where they could visit and chat while imbibing.

A group of 34 senile men in one situation were given a bottle of beer daily. After two months the whole atmosphere of the ward had changed. The number of incontinent men dropped from 26 to 9; jacket restraint required in 26 before the new regimen was required in only four afterward; the number of ambulatory patients rose from 7 to 25.

DEBATE OVER PSYCHOSURGERY INVOLVES PUBLIC AS WELL AS PHYSICIANS

CHICAGO — A treatment of the future or a horror from the past? What is psychosurgery and where is it going?

Psychosurgery is brain surgery — surgery to alter behavior. It has been the subject of much debate — pro and con — and some proposed legislation that would regulate the procedures.

Some 300 to 500 behavior-altering operations are done each year. There are 3,000 neurosurgeons in the United States. Some 95 per cent of their work involves head injuries, brain tumors, slipped discs and other conditions totally unrelated to psychosurgery. Operating time for a single psychosurgical procedure varies from two hours to five hours. Thus it is logistically impossible for psychosurgery to become a major factor in treatment of behavior problems.

Psychosurgery today is a highly refined cousin of the prefrontal lobotomy, which was introduced in the 1930s, only to be rejected almost totally (though not until an estimated 50,000 operations had been performed), the report says. The modern procedures have become a subject of discussion in scientific literature, lay publications, in Congress and in the courts.

AVERAGE AMERICAN PAYS DOCTOR'S \$209 YEARLY OUT-OF-POCKET

CHICAGO — How much do you personally pay out-of-po-

cket each year for medical costs?

That is — payments for your own care, not counting payments made in your behalf by insurance companies, employers, public agencies or others?

Average out-of-pocket spending for those Americans with medical costs in 1970 was \$209, says an article in *AMA Update*, a publication of the American Medical Association.

Nearly 88 per cent of the household population had some out-of-pocket outlays in the year for medical services or health insurance. About 12 percent had no out-of-pocket costs. About one-half the population had either no costs or costs of less than \$100.

About 2 per cent of the population, says *Update*, or some 4,000,000 people, had out-of-pocket expenses of \$1,000 or more in 1970.

The article is based on a survey by the National Center for Health Statistics, a branch of the U. S. Public Health Service.

THREE-FOURTHS OF NATION SEES DOCTOR EACH YEAR

CHICAGO — How often do you seek advice from or treatment by a doctor?

Most people — 72 per cent of the household population in 1971 — received a doctor's care or advice at least once during the year, says an article in *AMA Update*, a publication of the American Medical Association.

The average patient saw his doctor (or doctors) nearly seven times during the year, not including hospital visits.

How long does it take you to get to your doctor when you need him?

Patients in the survey reported an average travel time of about 17 minutes to the doctor's office, doorstep to doorstep.

Once you get to the doctor's office, how long must you wait before he sees you?

Average waiting time with an appointment was about half an hour, the *Update* report says. Without an appointment the average wait was nearly three-quarters of an hour.

The surveys were conducted by the National Center for Health Statistics, a branch of the U. S. Public Health Service.

FROM THE AMERICAN COLLEGE OF CHEST PHYSICIANS

CHICAGO — The Postgraduate Medical Education Committee of the American College of Chest Physicians announces its 1973 - 1974 Postgraduate Programs.

The ACCP in co-sponsorship with leading medical schools and teaching hospitals offer physicians and surgeons a continuing education program specializing in the diagnosis and treatment of heart and lung diseases. Each program will incorporate a variety of educational methods designed to

insure active student participation in the learning process.

The continuing education program for physicians sponsored by the American College of Chest Physicians has been accredited by the Council on Medical Education of the American Medical Association and is acceptable for credit toward the AMA Physician's Recognition Award.

For further information contact: Bradford W. Claxton, M. Ed., Director of Continuing Education, American College of Chest Physicians, 112 East Chestnut Street, Chicago, Illinois 60611.

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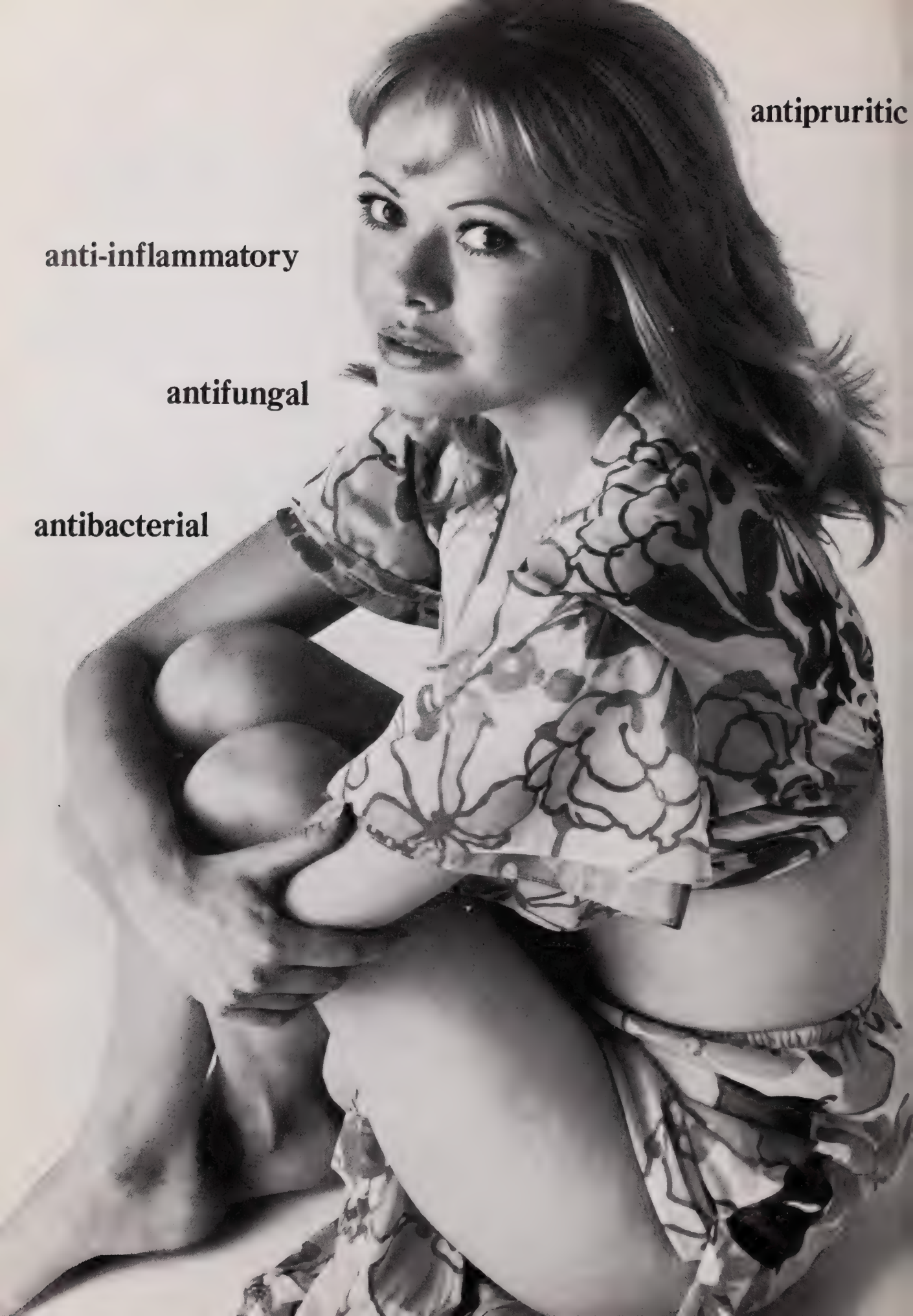
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Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, FDA has classified the indications as follows:

"Possibly" effective: Contact or atopic dermatitis; impetiginized eczema; nummular eczema; infantile eczema; endogenous chronic infectious dermatitis; stasis dermatitis; pyoderma; nuchal eczema and chronic eczematoid otitis externa; acne urticata; localized or disseminated neurodermatitis; lichen simplex chronicus; anogenital pruritus (vulvae, scroti, ani); folliculitis; bacterial dermatoses; mycotic dermatoses such as tinea (capitis, cruris, corporis, pedis); moniliasis; intertrigo.

Final classification of the less-than-effective indications requires further investigation.

CONTRAINDICATIONS

Hypersensitivity to Vioform-Hydrocortisone, or any of its ingredients or related compounds; lesions of the eye; tuberculosis of the skin; most viral skin lesions (including herpes simplex, vaccinia, and varicella).

WARNINGS

This product is not for ophthalmic use.

In the presence of systemic infections, appropriate systemic antibiotics should be used.

Usage in Pregnancy

Although topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use in pregnant females has not been established. Therefore, they should not be used extensively on pregnant patients in large amounts or for prolonged periods of time.

PRECAUTIONS

May prove irritating to sensitized skin in rare cases. If this occurs, discontinue therapy. May stain.

If used under occlusive dressings or for a prolonged period, watch for signs of pituitary-adrenal axis suppression.

May interfere with thyroid function tests. Wait at least one month after discontinuance of therapy before performing these tests. The ferric chloride test for phenylketonuria (PKU) can yield a false-positive result if Vioform is present in the diaper or urine.

Prolonged use may result in overgrowth of nonsusceptible organisms requiring appropriate therapy.

ADVERSE REACTIONS

Few reports include: Hypersensitivity, local burning, irritation, pruritus. Discontinue if untoward reaction occurs. Rarely, topical corticosteroids may cause striae at site of application when used for long periods in intertriginous areas.

DOSAGE

Apply a thin layer to affected areas 3 or 4 times daily.

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Cream, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearyl alcohol, cetyl alcohol, stearic acid, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of 5 and 20 Gm. **Ointment**, 3% iodochlorhydroxyquin and 1% hydrocortisone in a petrolatum base; tubes of 5 and 20 Gm. **Lotion**, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearic acid, cetyl alcohol, lanolin, propylene glycol, sorbitan trioleate, polysorbate 60, triethanolamine, methylparaben, propylparaben, and perfume Flora in water; plastic squeeze bottles of 15 ml. **Mild Cream**, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a water-washable base containing stearyl alcohol, cetyl alcohol, stearic acid, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of 1/2 and 1 ounce. **Mild Ointment**, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a petrolatum base; tubes of 1/2 and 1 ounce.

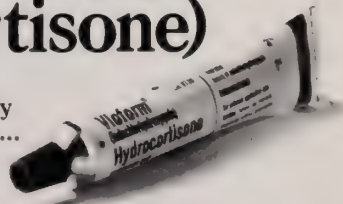
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Acido Ascórbico (C) (como ascorbato de sodio)	300 mg.
Niacinamida	100 mg.
Clorhidrato de Piridoxina (B-6)	2 mg.
Pantotenato de Calcio	20 mg.
Cobalamina (B-12) (como concentrado de cobalamina)	20 mg.
Vitamina E	30 Unidades Internacionales
Hierro (a partir de 50 mg. de sulfato ferroso)	10 mg.
Yodo (como yoduro de potasio)	0.15 mg.
Calcio (como carbonato)	50 mg.
Cobre (como sulfato)	1 mg.
Manganeso (como sulfato)	1 mg.
Magnesio (como sulfato)	6 mg.
Potasio (como sulfato)	5 mg.

Posología: Adultos y niños mayores de 6 años - 1 tableta diaria.

Presentación: Frascos de 30 y 90



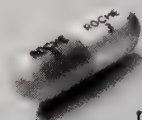
UPJOHN INTER-AMERICAN CORPORATION / CAPARRA / PUERTO NUEVO

PR 5226-1 MAY, 1969

6811 MARCA REGISTRADA EN E.U.A.: UNICAP THERAPEUTIC

How strong must a tranquilizer be for severe anxiety?

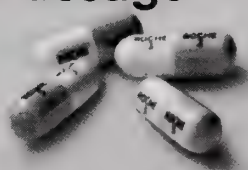
As strong as Librium® 25 mg (chlordiazepoxide HCl)



The achievement of desired therapeutic results is often a function of the dosage strength as well as the drug's intrinsic action. Thus, when anxiety is severe, the 25-mg strength of Librium frequently provides the necessary antianxiety action with a minimum of unwanted adverse reactions. Librium 25 mg is a convenient dosage form for the relief of severe, incapacitating anxiety, specifically formulated to supplement your counsel and reassurance.

Benefits-to-risks ratio permits higher dosage

For over 13 years, Librium has been recognized for its excellent benefits-to-risks ratio, an asset in the higher dosage ranges as in more common clinical applications. Thus, the frequency of dosage with Librium 25 mg can be flexibly adjusted to the needs and response of the individual patient, up to 100 mg daily if required. Total daily dosage for the elderly and debilitated should not exceed 20 mg. When severe anxiety has been reduced, Librium dosage should be correspondingly reduced or discontinued entirely.



basic support
in severe anxiety
Librium® 25 mg
(chlordiazepoxide HCl)
1 capsule t.i.d./q.i.d.



Roche Laboratories
Division of Hoffmann-La Roche Inc
Nutley, N.J. 07110

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Relief of anxiety and tension occurring alone or accompanying various disease states.

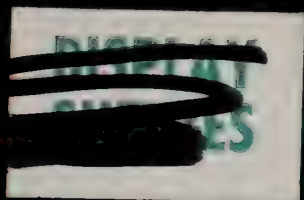
Contraindications: Patients with known hypersensitivity to the drug.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation, or in women of childbearing age requires that its potential benefits be weighed against its possible hazards.

Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

Supplied: Librium® Capsules containing 5 mg, 10 mg or 25 mg chlordiazepoxide HCl. Libritabs® Tablets containing 5 mg, 10 mg or 25 mg chlordiazepoxide.



DICIEMBRE 1973

VOL.65 NO.12



¡FELICIDADES!



Everybody experiences psychic tension.



Most people can handle this tension.



Some people develop excessive psychic tension and need your counseling,



and a few may need counseling
and the psychotropic action of Valium® (diazepam).

Before deciding to make Valium (diazepam) part of your treatment plan, check on whether or not the patient is presently taking drugs and, if so, what his response has been. Along with the medical and social history, this information can help you determine initial dosage, the possibility of side effects and the ultimate prospects of success or failure.

While Valium can be a most helpful adjunct to your counseling, it should be prescribed only as long as excessive psychic tension persists and should be discontinued when you decide it has accomplished its therapeutic task. In general, when dosage guidelines are followed, Valium is well tolerated (see Dosage). For convenience it is available in 2-mg, 5-mg and 10-mg tablets.

Drowsiness, fatigue and ataxia have been the most commonly reported side effects.

Until response is determined, patients receiving Valium should be cautioned against engaging in hazardous occupations requiring complete mental alertness, such as driving or operating machinery.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

Dosage: Individualize for maximum beneficial effect.

Adults: Tension, anxiety and psychoneurotic states, 2 to 10 mg b.i.d. to q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed; adjunctively in skeletal muscle spasm, 2 to 10 mg t.i.d. or q.i.d.; adjunctively in convulsive disorders, 2 to 10 mg b.i.d. to q.i.d. **Geriatric or debilitated patients:** 2 to 2½ mg, 1 or 2 times daily initially, increasing as needed and tolerated. (See Precautions.) **Children:** 1 to 2½ mg t.i.d. or q.i.d. initially, increasing as needed and tolerated (not for use under 6 months).

Supplied: Valium® (diazepam) Tablets, 2 mg, 5 mg and 10 mg; bottles of 100 and 500. All strengths also available in Tel-E-Dose® packages of 1000.



Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, N.J. 07110

Valium® (diazepam)

To help you manage excessive psychic tension

BOLETIN

ASOCIACION MEDICA DE PUERTO RICO



Organo Oficial

Fundado en 1903

Volumen 65

Diciembre 1973

Número 12

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acute arthritic inflammation...heat that freezes

In acute rheumatoid arthritis consider Tandearil. The anti-inflammatory action of Tandearil quickly helps reduce heat, pain, swelling, and stiffness. Results are usually seen in 3 or 4 days. Try it for a week when the symptoms defy aspirin control.

Remember that Tandearil is not a simple analgesic. It should not be used on patients responding to routine therapy. Before using, please read the prescribing information. It's summarized below.

Tandearil® helps take the heat off oxyphenbutazone NF Geigy

Tablets of 100 mg.

Important Note: This drug is not a simple analgesic. Do not administer casually. Carefully evaluate patients before starting treatment and keep them under close supervision. Obtain a detailed history, and complete physical and laboratory examination (complete hemogram, urinalysis, etc.) before prescribing and at frequent intervals thereafter. Carefully select patients, avoiding those responsive to routine measures, contraindicated patients or those who cannot be observed frequently. Warn patients not to exceed recommended dosage. Short-term relief of severe symptoms with the smallest possible dosage is the goal of therapy. Dosage should be taken with meals or a full glass of milk. Patients should discontinue the drug and report immediately any sign of: fever, sore throat, oral lesions (symptoms of blood dyscrasia); dyspepsia, epigastric pain, symptoms of anemia, black or tarry stools or other evidence of intestinal ulceration or hemorrhage, skin reactions, significant weight gain or edema. A one-week trial period is adequate. Discontinue in the absence of a favorable response. Restrict treatment periods to one week in patients over sixty.

Indications: Acute gouty arthritis, rheumatoid arthritis, rheumatoid spondylitis.

Contraindications: Children 14 years or less; senile patients; history or symptoms of G.I. inflammation or ulceration including severe, recurrent or persistent dyspepsia; history or presence of drug allergy; blood dyscrasias; renal, hepatic or cardiac dysfunction; hypertension; thyroid disease; systemic edema; stomatitis and salivary gland enlargement due to the drug; polymyalgia rheumatica and temporal arteritis; patients receiving other potent chemotherapeutic agents, or long-term anticoagulant therapy.

Warnings: Age, weight, dosage, duration of therapy, existence of concomitant diseases, and concurrent potent chemotherapy affect incidence of toxic reactions. Carefully instruct and observe the individual patient, especially the aging (forty years and over) who have increased susceptibility to the toxicity of the drug. Use lowest effective dosage. Weigh initially unpredictable benefits against po-

tential risk of severe, even fatal, reactions.

The disease condition itself is unaltered by the drug. Use with caution in first trimester of pregnancy and in nursing mothers. Drug may appear in cord blood and breast milk. Serious, even fatal, blood dyscrasias, including aplastic anemia, may occur suddenly despite regular hemograms, and may become manifest days or weeks after cessation of drug. Any significant change in total white count, relative decrease in granulocytes, appearance of immature forms, or fall in hematocrit should signal immediate cessation of therapy and complete hematologic investigation. Unexplained bleeding involving CNS, adrenals, and G.I. tract has occurred. The drug may potentiate action of insulin, sulfonylurea, and sulfonamide-type agents. Carefully observe patients taking these agents. Nontoxic and toxic goiters and myxedema have been reported (the drug reduces iodine uptake by the thyroid). Blurred vision can be a significant toxic symptom worthy of a complete ophthalmological examination. Swelling of ankles or face in patients under sixty may be prevented by reducing dosage. If edema occurs in patients over sixty, discontinue drug.

Precautions: The following should be accomplished at regular intervals: Careful detailed history for disease being treated and detection of earliest signs of adverse reactions; complete physical examination including check of patient's weight; complete weekly (especially for the aging) or an every two week blood check; pertinent laboratory studies. Caution patients about participating in activity requiring alertness and coordination, as driving a car, etc. Cases of leukemia have been reported in patients with a history of short- and long-term therapy. The majority of these patients were over forty. Remember that arthritic-type pains can be the presenting symptom of leukemia.

Adverse Reactions: This is a potent drug; its misuse can lead to serious results. Review detailed information before beginning therapy. Ulcerative esophagitis, acute and reactivated gastric and duodenal ulcer with perforation and hemorrhage, ulceration and perforation of large bowel, occult G.I. bleeding with anemia,

gastritis, epigastric pain, hematemesis, dyspepsia, nausea, vomiting and diarrhea, abdominal distention, agranulocytosis, aplastic anemia, hemolytic anemia, anemia due to blood loss including occult G.I. bleeding, thrombocytopenia, pancytopenia, leukemia, leukopenia, bone marrow depression, sodium and chloride retention, water retention and edema, plasma dilution, respiratory alkalosis, metabolic acidosis, fatal and nonfatal hepatitis (cholestasis may or may not be prominent), petechiae, purpura without thrombocytopenia, toxic pruritus, erythema nodosum, erythema multiforme, Stevens-Johnson syndrome, Lyell's syndrome (toxic necrotizing epidermolysis), exfoliative dermatitis, serum sickness, hypersensitivity angitis (polyarteritis), anaphylactic shock, urticaria, arthralgia, fever, rashes (all allergic reactions require prompt and permanent withdrawal of the drug), proteinuria, hematuria, oliguria, anuria, renal failure with azotemia, glomerulonephritis, acute tubular necrosis, nephrotic syndrome, bilateral renal cortical necrosis, renal stones, ureteral obstruction with uric acid crystals due to uricosuric action of drug, impaired renal function, cardiac decompensation, hypertension, pericarditis, diffuse interstitial myocarditis with muscle necrosis, perivascular granulomata, aggravation of temporal arteritis in patients with polymyalgia rheumatica, optic neuritis, blurred vision, retinal hemorrhage, toxic amblyopia, retinal detachment, hearing loss, hyperglycemia, thyroid hyperplasia, toxic goiter, association of hyperthyroidism and hypothyroidism (causal relationship not established), agitation, confusional states, lethargy; CNS reactions associated with overdosage, including convulsions, euphoria, psychosis, depression, headaches, hallucinations, giddiness, vertigo, coma, hyperventilation, insomnia; ulcerative stomatitis, salivary gland enlargement.

(B)98-146-800-F (10/71)

For complete details, including dosage, please see full prescribing information.

GEIGY Pharmaceuticals
Division of CIBA-GEIGY Corporation
Ardley, New York 10502

It's time for action to defend the laws and regulations that protect your patients against drug substitution.

These professional and trade organizations are united in supporting antisubstitution statutes and regulations:

The American Academy of Dermatology

The Board of Directors of the
American Academy of Family
Physicians

The Executive Board of the
American Academy of Neurology

The Committee on Drugs of the
American Academy of Pediatrics

The American College of Allergists

The Executive Committee of the
American College of Obstetricians
and Gynecologists

The Board of Regents of the
American College of Physicians

The Board of Trustees of the
American Dental Association

The Board of Trustees of the
American Medical Association

The American Psychiatric Association

The Executive Committee of the
National Association of Retail
Druggists

The Board of Directors of the
Pharmaceutical Manufacturers
Association

The National Wholesale Druggists'
Association



Joint Statement on Antisubstitution Laws and Regulations

The purpose of this statement is to affirm the support of the participating organizations for the laws, regulations and professional traditions which prohibit the unauthorized substitution of drug products.

Traditionally, physicians, dentists and pharmacists have worked cooperatively to serve the best interests of patients. Productive cooperation has been achieved through mutual respect as well as a common concern for the ideals of public service. This mutual respect has been reflected, in part, by joint support over the years for the adoption and enforcement of laws and regulations specifically prohibiting unauthorized substitution and encouraging joint discussion and selection of the source of supply of drug products. The basic principles of medical, dental and pharmacy practice are thus utilized and preserved in the interest of patient welfare.

The antisubstitution laws have not obstructed enhancement of the professional status of pharmacy any more than they have in and of themselves guaranteed absolute protection from unsafe drugs, or freed physicians, dentists and pharmacists from their responsibilities to patients. As a practical matter, however, such laws and regulations encourage inter-professional communications regarding drug product selection and assure each profession the opportunity to exercise fully its expertise in drug usage, to the advantage of patients.

Physicians and dentists should be urged to increase the frequency and regularity of their contacts with pharmacists in selection of quality drug products, recognizing that

economies to patients can be improved through such communication, taking into account the patients' needs. The pharmacist's knowledge of the chemical characteristics of drugs, their mode of action, toxic properties and other characteristics that assist in making drug selection decisions should be utilized to the fullest extent practicable by physicians and dentists in serving their patients.

Since drug product selection entails knowledge derived from clinical experience, the physician's and dentist's roles in product selection remain primary and do not permit delegation of decisions requiring medical and dental judgments. A broader role in therapy will evolve for pharmacists as improved understanding and cooperation among the professions continue to grow.

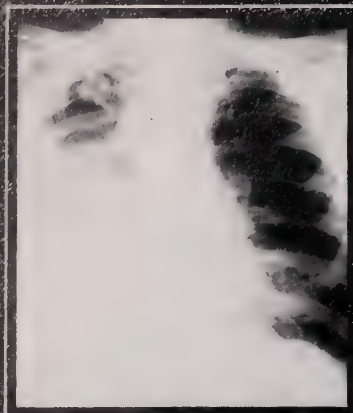
There has been no evidence that there are convincing reasons to modify or repeal existing laws and regulations prohibiting the unauthorized substitution of another drug product for the one specified by a prescriber. It is our belief that such laws and regulations merit the joint support of the medical, dental and pharmaceutical professions and the pharmaceutical industry.

Add your opinion to the weight of other professionals and send it to your state assemblyman or legislator.

*Pharmaceutical Manufacturers Association
1155 Fifteenth Street, N.W., Washington, D. C. 20005*



HERE Pleural effusion




Wherever it hurts,
Empirin Compound with
Codeine usually provides
the relief needed.

HERE Biliary calculi



In general, only pain so severe
that it requires morphine is
beyond the scope of
Empirin Compound with Codeine.

 **prescribing convenience:**
up to 5 refills in 6 months,
at your discretion (unless
restricted by state law); by
telephone order in many states.

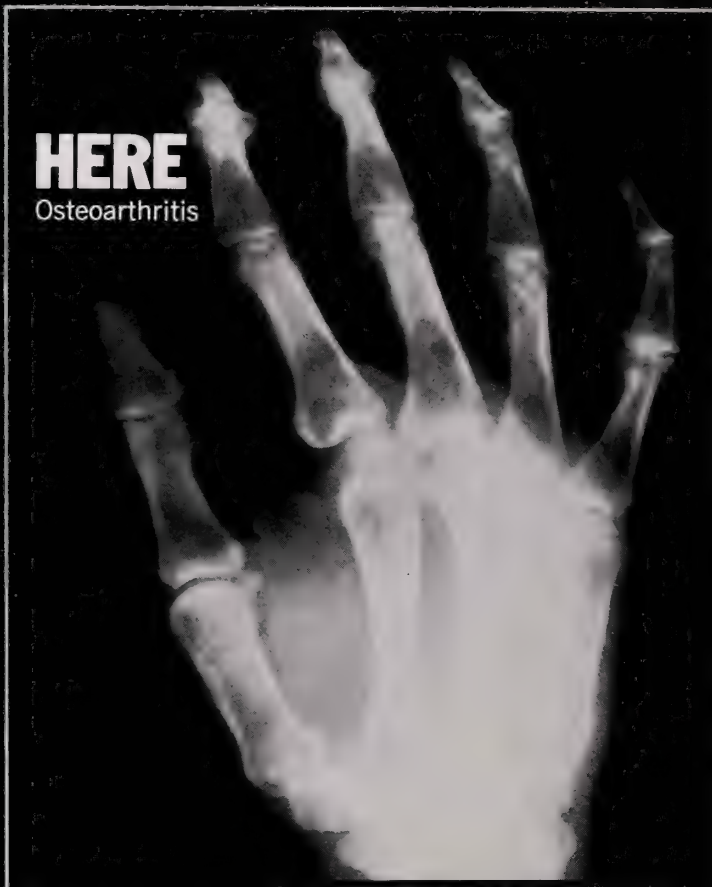
Empirin Compound with
Codeine **No. 3**, codeine
phosphate* 32.4 mg. (gr. ½);
No. 4, codeine phosphate*
64.8 mg. (gr. 1). *Warning—
may be habit-forming. Each
tablet also contains: aspirin
gr. 3½, phenacetin gr. 2½,
caffeine gr. ½.



Burroughs Wellcome Co.
Research Triangle Park
North Carolina 27709

WHEREVER IT HURTS

HERE
Osteoarthritis



EMPIRIN COMPOUND c CODEINE

#3, codeine phosphate* (32.4 mg.) gr. ½
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INFANT**

Whenever the
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TOO.**



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the soft underbelly
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For Obesity...
a unique short-term
adjunct to diet
and counseling

New
Sanorex[®]
(mazindol)
TABLETS, 2 mg.

A different chemical
structure

Some distinctive
pharmacologic differences

Demonstrable clinical
efficacy

One-a-day dosage



For Brief Summary, please see last
page of this advertisement.

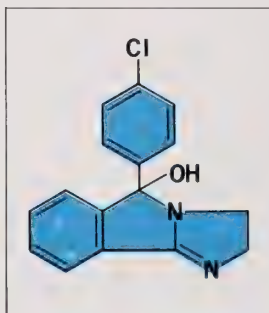
Facts about new Sanorex® (mazindol)

A short-term adjunct in the treatment of exogenous obesity

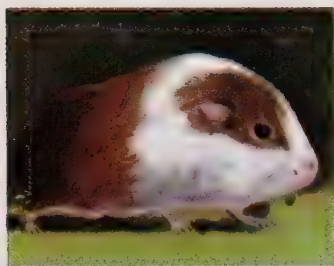
Sanorex is indicated in the management of exogenous obesity as a short-term (a few weeks) adjunct in a regimen of weight reduction based on caloric restriction. When diet and counseling are felt to be insufficient, the addition of Sanorex to the regimen may prove helpful.

Unique chemical structure among anorexiant

Sanorex (mazindol) is an imidazo-isoindole anorexi-ant chemically unrelated to amphetamine and other sympathomimetic phenethylamines. Chemically designated as 5-p-chlorophenyl-5-hydroxy-2,3-dihydro-5H-imidazo [2,1-a] isoindole, it has the following structure.



Some pharmacologic similarities to amphetamines... and some differences



Sanorex has pharmacologic activity similar in many ways to that of amphetamines, including central nervous system stimulation in humans and animals, as well as such amphetamine-like effects in animals

as the production of stereotyped behavior. Animal experiments also suggest certain differences from amphetamines.

1) Site of Action—Limbic System vs. Hypothalamus

In animal experiments, Sanorex appears to exert its primary effects on the limbic system of the brain, whereas amphetamine acts upon hypothalamic and midbrain structures.*

2) Effect on Norepinephrine

Unlike amphetamine, Sanorex does not cause depletion of brain norepinephrine in animals;* on the other hand, it does appear to inhibit storage-site uptake of norepinephrine as is suggested by its marked potentiation of the effect of exogenous norepinephrine on blood pressure in dogs and on smooth muscle contraction *in vitro*.

*The significance of these differences for humans is uncertain.

Clinical studies of weight loss with Sanorex (mazindol)

The average magnitude of increased weight loss of drug-treated patients over placebo-treated patients in studies of anorexiant in general is ordinarily only a fraction of a pound a week. In clinical studies of Sanorex, the average weight loss per week for Sanorex over placebo is significant. The rate of weight loss is greatest in the first weeks of therapy for both drug and placebo subjects and tends to decrease in succeeding weeks.

Double-blind clinical trials were conducted with a total of 3858 patients, 2183 of these receiving Sanorex on varying dosage schedules. In these studies, 587 patients received Sanorex for a period of 6 weeks in recommended dosages (462 patients, 1 mg. t.i.d. and 125 patients, 2 mg. o.d.) and 451 patients received placebo.

While the weight loss associated with Sanorex has been generally consistent within individual clinical trials, the amount varies, as with other agents, from trial to trial. This variance appears to be related in part to variables other than the agents prescribed, such as the interaction between physician-investigator and the patient, the population treated, and the diet prescribed. The importance of nondrug factors in such weight loss has not been elucidated.

Simplicity of dosage helps patients follow regimen

One 2-mg. tablet per day taken one hour before lunch. That's it. This one-a-day dosage can help many patients—who might otherwise tire of and become discouraged with a regimen.

Administration is flexible, however. For the patient in whom it is preferred, 1-mg. 3 times daily, one hour before meals, may be prescribed. Sanorex is supplied as 2-mg. scored tablets to facilitate these regimens.

Rx _____
*Sanorex Tablets
#40
1 Tablet one hour
before lunch*

Tolerance and dependence

Sanorex shares important pharmacologic properties with amphetamines. Amphetamines and related stimulant drugs have been extensively abused and can produce tolerance and severe psychologic dependence. In this regard, the manifestations of chronic overdosage or withdrawal of Sanorex have

not been determined in humans. Abstinence effects have been observed in dogs after abrupt cessation for prolonged periods. There was some self-administration of the drug in monkeys. While the abuse potential of Sanorex has not been clearly defined, the possibility of dependence should be kept in mind when evaluating the desirability of including Sanorex as part of a weight-reduction program.

Indication: In exogenous obesity, as a short-term (a few weeks) adjunct in a weight-reduction regimen based on caloric restriction. The limited usefulness of agents of this class should be measured against possible risk factors.

Contraindications: Glaucoma; hypersensitivity or idiosyncrasy to the drug; agitated states; history of drug abuse; during, or within 14 days following, administration of monoamine oxidase inhibitors (hypertensive crises may result.)

Warnings: Tolerance to many anorectic drugs may develop within a few weeks; if this occurs, do not exceed recommended dose, but discontinue drug. May impair ability to engage in potentially hazardous activities, such as operating machinery or driving a motor vehicle, and patient should be cautioned accordingly.

Drug Interactions: May decrease the hypotensive effect of guanethidine; patients should be monitored accordingly. May markedly potentiate pressor effect of exogenous catecholamines; if a patient recently taking mazindol must be given pressor amine agents (e.g., levarterenol or isoproterenol) for shock (e.g., from a myocardial infarction), extreme care should be taken in monitoring blood pressure at frequent intervals and initiating pressor therapy with a low initial dose and careful titration.

Drug Dependence: Mazindol shares important pharmacologic properties with amphetamines and related stimulant drugs that have been extensively abused and can produce tolerance and severe psychologic dependence. Manifestations of chronic overdose or withdrawal with mazindol have not been determined in humans. Abstinence effects

have been observed in dogs after abrupt cessation for prolonged periods. There was some self-administration of the drug in monkeys. EEG studies and "liking" scores in human subjects yielded equivocal results. While the abuse potential of mazindol has not been further defined, possibility of dependence should be kept in mind when evaluating the desirability of including the drug in a weight-reduction program.

Usage in Pregnancy: In pregnancy or women who may become pregnant, potential benefit must be weighed against possible hazard to mother and infant.

Usage in Children: Not recommended for use in children under 12 years of age.

Precautions: Insulin requirements in diabetes mellitus may be altered. Smallest amount of mazindol feasible should be prescribed or dispensed at one time to minimize possibility of overdose. Use cautiously in hypertension, with monitoring of blood pressure; not recommended in severe hypertension or in symptomatic cardiovascular disease including arrhythmias.

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Julian Katz, M.D.
*Assistant Professor of
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Gastrin: an updated look at an important hormone

Early in this century Edkins showed that the intravenous injection of an extract of antral mucosa would stimulate gastric acid secretion. He gave the name gastrin to this proposed hormone. After Komarov substantiated the presence of such a hormone, Gregory and fellow workers isolated, characterized, and synthesized the polypeptide. Gastrin not only has an important influence on acid secretion, but also plays a major role in other gastrointestinal functions.

Structure

Antral gastrin contains 17 amino acids. It is remarkable that a 4 amino acid segment, the carboxyl terminal portion, can reproduce all the activities of which the whole molecule is capable.

Gastrin and feedback mechanism of acid secretion

Gastrin is produced primarily by the mucosal cells in the gastric antrum, the distal non-acid secreting portion of the stomach. The hormone stimulates the parietal cells in the fundus and body of the stomach to produce acid, and a negative feedback mechanism is initiated. Acid bathing the antrum acts directly on the gastrin-producing cell to inhibit release of the hormone.

Gastrin and the lower esophageal sphincter

Contraction of the gastroesophageal sphincter is stimulated by

gastrin. The sphincter muscle is more sensitive to the effects of gastrin than adjacent esophageal muscle. The efficacy of antacid therapy in reflux esophagitis may be due, in part, to the release of antral gastrin. Antacids neutralize gastric acid and raise the pH in the antrum. The gastrin which is then released increases the strength of the sphincter, which acts as a barrier against reflux.

Some other actions of gastrin

Beyond gastrin's prime role as a stimulator of gastric acid production, gastrin also acts on other parts of the G.I. tract. On the stomach, to stimulate (albeit weakly) pepsin production and increase gastric antral motility. On the pancreas, by stimulating enzyme secretion. On the liver, by increasing the flow of bile. On the intestine, by inhibiting absorption of water and electrolytes, and—possibly—increasing motility. And, on the ileocecal sphincter, by relaxing it (contrary to its action on the gastroesophageal sphincter), and perhaps contributing to the gastro-colic reflex.

Excessive gastrin production

It would be expected that if the stomach could not produce acid, gastrin release would continue unabated. Indeed such is the case in pernicious anemia, where there is achlorhydria, and circulating gastrin levels are very high. Alka-

linization of the antrum, vagal stimulation, and mechanical distension of the antrum all provoke gastrin release.

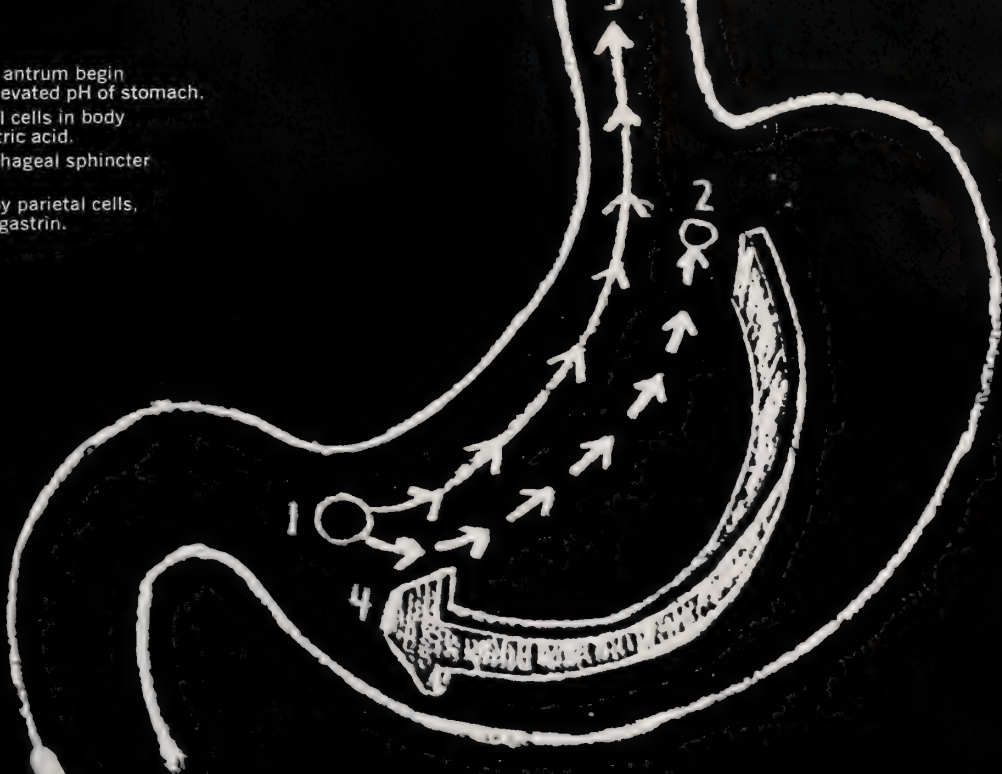
In the Zollinger-Ellison syndrome the radioimmunoassay of gastrin may be the best diagnostic technique. The islet-cell tumor produces large amounts of gastrin, leading to gastric hypersecretion and often intractable ulcer disease. Another situation in which gastrin levels may be high, is when the antrum is retained after gastric resection. Here the antrum is removed from the inhibitory effects of acid, and hypersecretion of gastrin occurs.

Some therapeutic implications

Obviously surgical removal of the antrum will lower gastric secretion as therapy for peptic ulcer disease. But other ways of antagonizing gastrin are being investigated. Some substances have a close structural similarity to the gastrin molecule. For example, cholecystokinin, the intestinal hormone, and caerulein, a material extracted from the skin of amphibians, contain in their structure a sequence of amino acids identical to the active terminal portion of gastrin. These substances are competitive inhibitors of gastric secretion. They combine with the receptor site for acid secretion, cause little stimulation of the receptor, and thus occlude the site.

Keys

1. Gastrin-producing cells in antrum begin secreting in response to elevated pH of stomach.
2. Gastrin stimulates parietal cells in body and fundus to secrete gastric acid.
3. Contraction of gastroesophageal sphincter facilitated by gastrin.
4. Resulting HCl, produced by parietal cells, inhibits further release of gastrin.



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LA PRUEBA EN LAMINA DE 3 MINUTOS QUE DETECTA EL EMBARAZO



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PROGRESO TERAPEUTICO:

DIAGNOSTICO Y MANEJO DE ENDOCARDITIS INFECCIOSA

Carlos H. Ramírez Ronda, MD

Los artículos para esta Sección deben ser breves y presentar el material condensado y en una forma clara, usando tablas o gráficas para ilustrar los aspectos sobresalientes. Se requerirá que sean de no más de 7 páginas a doble espacio. Se estimulará a que sean en español con excepción de aquellos escritos por autoridades de habla inglesa. Los artículos tendrán una breve lista de libros o artículos recomendados para el que desee estudiar más el tema.

Las enfermedades infecciosas del endocardio se han estudiado repetidamente y varias monografías han aparecido periódicamente. Afortunadamente el manejo de esta condición ha mejorado drásticamente durante la era antibiótica.

La frecuencia de casos probados bacteriológicamente ha disminuído en los años recientes. Kerr reportó que en "Charity Hospital" de New Orleans, en el período entre 1946-1956, ocurrieron 25 casos por año, mientras que entre 1957-1963 solo ocurrieron 4 casos por año. En general, la incidencia es de uno por cada 4,000 admisiones al hospital. La edad promedio para endocarditis bacteriana (EB) se ha reportado como 49.7 años, mientras que para endocarditis bacteriana sub-aguda (EBS) es 57 años. Una observación de importancia es que el 60 por ciento de los pacientes con esta condición es sobre los 50 años de edad. Los varones predominan a las mujeres en razones de 2:1 a 5:1. Debe de acentuarse el hecho de que hay preponderancia para varones más viejos y una tendencia para las mujeres a tener EB a una edad más temprana.

Del Departamento de Medicina del Hospital de Distrito Universitario y la Escuela de Medicina de la Universidad de Puerto Rico.

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Favor de pedir reproducciones a: Carlos H. Ramírez-Ronda, MD, Box 35465, Dallas, Texas, 75235.

Microbiología

Thompsett reportó que el 90 por ciento de los casos de EB eran causados por estreptococos. Las especies aisladas en 86 pacientes fueron las siguientes: Streptococcus viridans en 27, microaerófilico en 13, anaeróbico en 3, enterococo en 8 y no hemolítico en 2. En diferentes series los estafilococos son responsables del 20 por ciento al 30 por ciento de los casos de endocarditis infecciosa (EI); más del 50 por ciento de los casos de endocarditis bacteriana aguda (EBA) la causa el estafilococo. En las pasadas dos décadas, la incidencia de endocarditis estafilococcica ha aumentado. Entre los factores que contribuyen al aumento en la incidencia es que Staphylococcus aureus es el agente etiológico más común en la endocarditis de los adictos a heroína y que este agente es una complicación prominente en cirugía cardíaca. El estafilococo más común es el aureus, cuando albus está presente usualmente ocurre en pacientes con enfermedad reumática del corazón. El neumococo y gonococo que fueron agentes etiológicos frecuentes en la era pre-antibiótica ahora sólo son responsables por el 1 por ciento al 5 por ciento de los casos. EB puede ser causada por organismos no comunes y se dice que entre el 5 por ciento y 10 por ciento de los casos se deben a estas bacterias. Algunas de las bacterias reportadas son: Listeria monocytogenes, Micrococcus tetragens, Bacteroides, Mima, Serratia, Brucella y otros.

Los hongos pueden causar EI. La endocarditis por hongos usualmente ocurre en pacientes inmunosuprimidos, en pacientes después de cirugía cardiovascular y en adictos a narcóticos. Candida e Histoplasma son responsables por el 33 por ciento de los casos. Candida es el agente etiológico en una tercera parte de los casos post quirúrgicos. Una cuarta parte de los pacientes con endocarditis de hongos es el resultado de superinfección en un paciente en regímenes de antibióticos prolongados. De significado clínico es que en este tipo de endocarditis ocurre frecuentemente embolización a las arterias mayores especialmente las extremidades inferiores.

Uno de los aspectos más estimulantes es la identifica-

ción del lugar de entrada del microorganismo. En EBA es más fácil documentar una fuente extracardiaca de infección como son los adictos que usan las vías endovenosas, infecciones en los dientes, genitalia o piel; instrumentación genitourinaria y procedimientos quirúrgicos o ginecológicos. Para EBS la puerta de entrada es usualmente no aparente, más los factores que predisponen son: infecciones respiratorias, manipulaciones dentales, infecciones del tracto urinario, partos, abortos, trauma, sondeos cardíacos, quemaduras, otitis y sinusitis. Para EBS el cuadro clínico incluye a un paciente con una lesión cardíaca previa.

Manifestaciones Clínicas

El signo más frecuente de EI es fiebre, las personas de edad avanzada pueden no tener fiebre. La fiebre puede ocurrir en pacientes que se sospeche EBS sin ser ésta la etiología como en caso de exacerbación de enfermedad reumática en la ausencia de EB. Soplos significativos se encuentran en el 99 por ciento de los casos de EBS con daño valvular previo. Soplos cambiantes descritos clásicamente en EBS pueden ocurrir en EBS como en EBA. Un problema que reta se le presenta al clínico con endocarditis del lado derecho en donde los soplos pueden estar ausentes en dos terceras partes de los pacientes. ¿Puede EB ocurrir en la ausencia de soplos? La contestación es sí. Como grupo entre el 15 por ciento y 20 por ciento de los pacientes con EB no tienen soplos a la auscultación.

La piel es el órgano más grande del cuerpo, por lo tanto manifestaciones de EI tienen que verse en esta gran pantalla. Las petequias son comunes, antes de la era antibiótica ocurrían en 26 por ciento al 86 por ciento de los casos, más después de la introducción de antibióticos bajó al 29 por ciento. Un bazo palpable se encuentra más frecuentemente en EBS que en EBA con una incidencia de 44 por ciento y 23 por ciento respectivamente. Cuando se busque el bazo debe uno acordarse que es palpable en menos de la mitad de los pacientes con EI. Dedos en palillos de tambor que en la era pre-antibiótica se veían entre el 43 por ciento y 68 por ciento de los pacientes, hoy se ven solo en el 7 por ciento de los pacientes con EB.

Las complicaciones de EB pueden dar manifestaciones clínicas específicas. Fenómenos embólicos son frecuentes en EBS con una incidencia de 33 por ciento que se ha mantenido constante. Embolias al bazo ocurren en 44 por ciento de los pacientes. Embolias a las coronarias ocurren en un 60 por ciento de los casos, la mayoría de las cuales pasan desapercibidas.

Se han reportado casos de oclusión de la arteria retiniana central. En un paciente con endocarditis, del lado derecho el lugar más común de embolia es el pulmón y en algunos casos ocurren abscesos pulmonares.

Hematuria puede ocurrir en 37 por ciento al 86 por ciento de los casos de EBS; sin embargo, la etiología no es necesariamente embólica y sí mayormente inmunológica. Una presentación rara de EBS es fallo renal agudo en donde el diagnóstico histológico es una glomerulitis secundaria a EB.

Las manifestaciones neurológicas varían. Jochmann dijo "hemiplegia en un adulto joven siempre piensa en EBS". Manifestaciones neurológicas centrales ocurren en el 20 por ciento de los casos, varían de meningitis estéril a hemiplegia secundaria a infarto post embolia, a un absceso cerebral manifestándose como cambios en comportamiento en casos de EBA.

Las complicaciones cardiovasculares son las manifestadas por fallo de la bomba. Cuando un paciente con EB comienza a desarrollar fallo cardíaco debe tratarse inmediatamente y ser observado muy de cerca. De los pacientes que sucumben a la enfermedad entre el 50 por ciento y 60 por ciento tuvieron fallo cardíaco.

Hallazgos de Laboratorio

Como cualquier otro paciente, aquellos con EI deben ordenársele las pruebas rutinarias. El urinalisis demostrará hematuria y proteinuria en 60 por ciento de los pacientes. El 50 por ciento de los pacientes en Estados Unidos tienen un hematocrito de 38 por ciento o menos. Anemia ocurre en el 50 por ciento al 80 por ciento de los casos con la enfermedad. El frotis de sangre periférica puede revelar preponderancia de histiocitos y la velocidad de sedimentación está aumentada en 90 por ciento de los casos. El factor reumatoideo (FR) está presente en el 50 por ciento de los casos.

El cultivo de sangre es la ayuda más importante para el diagnóstico. El número óptimo de cultivos es 5 o 6 y la razón de medio de cultivo a sangre debe ser de 20:1, esto es alrededor de 5 cc de sangre por botella de cultivo que tenga 100cc (3.3 onzas) de medio de cultivo. Los cultivos deben tomarse aerobicamente y anaerobicamente y ser incubados por lo menos 2 a 3 semanas. Si el paciente recibió penicilina G, añádase 150 unidades de penicilinas por 5 cc de medio de cultivo y si se usó una penicilina resistente a penicilinas deben añadirse 8,000 unidades de penicilinas por 5 cc de medio de cultivo. Las sulfonamidas y tetraciclinas deben neutralizarse con ácido para-aminobenzoico y cistina respectivamente.

Una vez se haya cultivado e identificado el organismo,

GUIA PARA EL MANEJO DE ENDOCARDITIS

1. Piense en la posibilidad de endocarditis en presencia de fiebre y un soplo cardíaco.
2. Sospeche endocarditis en presencia de fiebre, soplo cardíaco y esplenomegalia o petequias o evidencia de embolización.
3. Diagnostique endocarditis cuando 1 o 2 está presente y un organismo se aísla de la sangre.
4. Haga:
 - A. Cinco cultivos de sangre 2 o más horas aparte (5 cc sangre por cultivo).
 - B. Añada penicilinas a la botella de cultivo si el paciente ha recibido penicilina.
 - C. Si el organismo se aísla, guárdelo. Haga sensibilidades en tubo de dilución.
 - D. Periódicamente conteje de blancos y hematocrito, orinas diarias, función renal semanal, placa de pecho y ECG semanalmente.
5. No haga:
 - A. Comenzar tratamiento y luego abandonarlo antes del período recomendado.
 - B. Comience tratamiento sin cultivos de sangre.
6. Tratamiento:
 - A. Si la enfermedad ha persistido más de 4 semanas y el paciente no está desesperadamente enfermo espere 3 a 4 días hasta que el organismo se identifique.
 - B. Escoja penicilina G para tratamiento cuando sea posible.
 - C. Después de 24 a 48 horas de tratamiento, use diluciones bactericidas del suero en contra del organismo aislado. Si los antibióticos o ruta de administración se cambia, se repite la prueba. Por lo menos se requiere una dilución de 1:4 o 1:8.
 - D. Trate por tiempo suficiente.
7. Problemas de tratamiento:
 - A. Falta de mejorar la fiebre (causas posibles)
 1. Antibiótico es no efectivo: ruta, dosis, otros antibióticos
 2. Respuesta lenta (estafilococo 7 días)
 3. Absceso: lugar de inyección, riñón, bazo
 4. Alergia al antibiótico (erupción en piel, eosinofilia, dolores articulares)
 - B. Nueva fiebre:
 1. Embolo
 2. Superinfección
 3. Alergia a antibióticos
 4. Flebitis
 - C. Desarrollo de fallo cardíaco
 1. Ruptura de cúspide aórtica
 2. Sobredosis de sodio. Cotejar los líquidos

estudios de sensibilidad deben llevarse a cabo. La sensibilidad de discos es adecuada en la mayoría de los casos, más cuando se encuentra dificultad, sensibilidades por tubos de dilución deben llevarse a cabo. Una vez se comience en terapia basada en estudios de sensibilidad, el nivel bactericida del suero debe determinarse. Usando el método de Schlichter, si el suero es bactericida para el organismo del paciente en una dilución de 1:8 o mayor, la dosificación está adecuada y la posibilidad de relapso después de discontinuar terapia es menos probable.

Terapia

La terapia de EB o EI depende mayormente del agente etiológico y la dosificación se ajusta de acuerdo

al nivel bactericida en suero. Todos los pacientes con endocarditis deben estar hospitalizados e informados que estarán hospitalizados de 4 a 8 semanas. La manera mejor de administrar antibióticos es por vía endovenosa usando una aguja de mariposa 21-23 G, en forma intermitente cada 4-6 horas. La terapia de un caso que se sospecha EBA debe comenzarse inmediatamente después de tomar los cultivos con una penicilina resistente a penicilinas como lo es metilicina y oxacilina en dosis de 12-20 gramos endovenoso (EV) por día, por un período de tiempo de 6 a 7 semanas; como alternativa puede usarse vancomicina (Vancocin) 2 gramos EV por día. Cuando sospeche EBS y el paciente no está agudamente enfermo, una corta espera por los resultados del cultivo

antes de comenzar terapia está indicado ya que una vez se comience terapia en base empírica debe continuarse por 4 a 6 semanas. El antibiótico a usarse cuando posible es penicilina, si el organismo es *Streptococcus viridans* debe usarse penicilina G de 10-20 millones EV por día, durando la terapia 4 semanas. Si el organismo es *Streptococcus fecalis* debe usarse penicilina G 20-40 millones de unidades por día EV más estreptomycin 2 gramos intramuscular (IM) por día, y la terapia durará de 6 a 7 semanas. Cuando no se cultiva ningún organismo se comienza con penicilina 10 millones unidades por día más estreptomycin 2 gramos IM por día, si no hay respuesta clínica en 72 horas se dobla la dosis de penicilina cada 48 horas hasta llegar a 40 millones de unidades o 6 días de terapia, de no haber respuesta se añade una penicilina resistente a penicilinasas en dosis de 12 a 20 gramos EV por día. Cuando se encuentra un organismo gram negativo, terapia con gentamicina (Garamycin) 5 mg./kg./día más cefalotina (Keflin) o ampicilina 8 gramos EV por día debe comenzarse inmediatamente. Si se sospecha infección con *Pseudomonas* el uso de gentamicina más carbenicilina (Pyopen) 30 gramos/día EV está indicado. El tratamiento de endocarditis por hongos requiere amfotericina B, 1mg./kg./día para llegar a un total de 25 mg./kg. Si endocarditis de hongos ocurre después de cirugía cardíaca el tratamiento es remoción quirúrgica de las vegetaciones.

En casos de endocarditis después de reemplazo de válvulas el organismo usualmente es *Staphylococcus epidermidis* y el tratamiento es médico como arriba discutido, a menos que ocurra embolismos sistémicos con compromiso hemodinámico. En esta etapa, el reemplazo quirúrgico de la válvula está indicado con cubierta adecuada de antibióticos.

El manejo quirúrgico de los pacientes con EI tiene su lugar y sus indicaciones. Un paciente con EI, que

desarrolla fallo cardíaco rápido, progresivo e intratable que no responde a manejo médico adecuado y apropiado, es un candidato para reemplazo de válvula, al igual que el paciente con embolias sistémicas o pulmonares recurrentes y aquellos pacientes cuya infección no responde y tienen sepsis severa.

Para terminar el mejor tratamiento de EI es la prevención aquellos pacientes que tengan enfermedad reumática del corazón que vayan a someterse a extracción dental, cirugía de oídos, nariz y garganta, o manipulaciones urológicas deben recibir profilácticamente desde el día del procedimiento hasta dos días después 600,000 unidades de penicilina procainada IM dos veces al día, y estreptomycin 1 gramo IM diario.

Reconocimiento

Quiero expresar mi agradecimiento al Dr. Mario R. García Palmieri por revisar el manuscrito, su ayuda, consejo y estímulo y al Dr. Norman Maldonado por revisar y corregir el manuscrito y hacer sugerencias muy valiosas.

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Nota: Lista de referencias completas disponibles del autor.

EVALUACION DE INCAPACIDAD LUMBOSACRAL

Herman J. Flax-Jaffe, MD, FACP

"Los cambios degenerativos de la columna vertebral no ocurren solamente en los huesos."

El balance postural para mantener una posición erecta es una lucha constante entre la fuerza de gravedad y tres grupos de músculos: los abdominales y los flexores de la cadera, los extensores de la espalda y de la cadera, y los poderosos tendones de la corva. Al fin, siempre la fuerza de gravedad vence, porque los músculos se debilitan. Pero, el hombre contribuye a este mal mantenimiento la "posición fetal" durante todo el día, y esto conlleva a unos músculos abdominales estirados, una espalda debilitada y unos tendones de la corva contraídos. Aun cuando duerme, lo hace en un colchón flexible y lujoso, que no le ayuda a sostener los tejidos blandos, causando así un continuo debilitamiento y estiramiento de los músculos y ligamentos de la espalda.

Cambios degenerativos, inevitables en la vida, no ocurren solamente en los huesos de la espalda. Los tejidos blandos se degeneran mucho más rápidamente que la estructura ósea. Aun así solo se le da atención, usualmente, a los cambios radiológicos del sistema esquelético. Sería muy difícil encontrar a una persona de edad mediana a quien no le duela la espalda; lo cual sería fácil achacárselo a alguna lesión durante el trabajo.

Esto es lo que precisamente hace muy difícil determinar el porcentaje de incapacidad luego de trauma a la espalda. Una evaluación lumbosacral basada únicamente en la presencia de dolor continuo en la espalda, es un verdadero error. Cuánto se debe a la lesión, y cuánto a una condición preexistente agravada, es un dilema difícil de resolver, a menos que el observador haya seguido de cerca el empleado desde el examen médico pre-empleo y cuenta con un conocimiento completo

de su historial como empleado y del tratamiento de la lesión actual.

La evaluación de la incapacidad tiene que considerar el tipo de accidente y el tratamiento. El factor más importante en el tratamiento es, sin duda, descanso en cama en un colchón firme hasta que desaparezcan todos los signos de espasmo muscular y de la contractura refleja de los músculos.

Esto hay que seguirlo con un programa gradual de ejercicios, ambulación, y retorno al trabajo. Este programa no tiene tiempo definido. Depende enteramente de los hallazgos físicos y síntomas del paciente, cuando se le hace el examen. ¿Si en un adolescente tomara tres semanas en curarse un esguince muscular o una ruptura de ligamento en condiciones óptimas, tomaría más o menos lo mismo en una persona de cincuenta años?

Cuando entran en juego las fuerzas y los esfuerzos de postura y de los halones musculares luego de una laminectomía para herniación del núcleo pulposo, es imposible precisar el tiempo en que desaparecerá el dolor. Es suficiente decir que ningún paciente se debe dar de baja de tratamiento activo, a menos que no hayan desaparecido de los músculos todos los signos físicos de espasmos y de contractura refleja de los músculos. Es mucho más seguro y más práctico permitirle más descanso en cama que menos descanso en estos pacientes.

La razón usual para que se prolonguen los síntomas, una gran recompensa final por incapacidad y con posible pérdida del trabajador para la industria, es precisamente, darlo de baja antes que los músculos envueltos estén más estirados y fuertes y sin tener un entendimiento absoluto de la postura para evitar una recaída en dolor de espalda. La ausencia de tratamiento adecuado y el darle de baja temprano son factores que hay que considerar en la evaluación de incapacidad debido a trauma a la espalda.

La naturaleza del trabajo es otro punto importante para determinar la incapacidad. No es justo considerar la misma incapacidad en un oficinista que desarrolla un disco herniado levantando una maquinilla, que en un estibador que desarrolla el suyo cargando un saco de cien libras de azúcar. El primero puede volver a su trabajo sin dificultad mientras que el segundo

tiene que buscar otro empleo. Aunque ambos probablemente tengan la misma incapacidad desde el punto de vista de pérdida en poderío muscular y amplitud de movimiento de las articulaciones.

Si hay duda de que el paciente pueda tener dificultad para reintegrarse a su trabajo, se le debe someter a una prueba de trabajo como parte de su tratamiento antes de darlo de baja. En esta prueba las condiciones de trabajo se duplican y se evalúa al paciente en su habilidad para hacer este trabajo. Los signos físicos se parean con los cambios en síntomas, porque es difícil evaluar la queja subjetiva de dolor, que es una característica individual. Por regla general, el dolor es peor, si hay factores psicológicos y/o económicos envueltos. Por esta razón, la prueba de trabajo brinda la contribución más valiosa al centro de rehabilitación para determinar el impedimento vocacional del paciente con incapacidad lumbosacral.

Una persona afectada por el síndrome de dolor de espalda no debe volver a un trabajo que le haga más daño a esta área. Rehabilitación vocacional es esencial para estos individuos. Es muy difícil para una persona de edad avanzada encontrar un trabajo nuevo. ¡A veces es difícil para un joven! Si el individuo puede conseguir un trabajo con el mismo salario, la evaluación de la incapacidad final no debe ser la misma que la de un trabajador que no se puede entrenar. Sin embargo, se le debe ofrecer ayuda económica al trabajador durante el período de entrenamiento vocacional.

No es sorprendente la forma en que muchos obreros son estimulados por la compensación monetaria que les brinda su lesión. Esto es más evidente en una región donde escasean las oportunidades de empleo. La mayoría de estos casos no se mejorarán hasta que todas las peripecias de la jurisprudencia local hayan sido agotadas. Quizás, es por esta razón que en algunas reclamaciones la evaluación original de incapacidad sea muy baja. Uno no puede esperar una decisión diferente, no importa cuan alto sea el porcentaje de incapacidad autorizada, si es la costumbre local apelar cualquier decisión, y la regla general de la corte superior a aumentar el mismo.

Un negocio, y una compañía de seguro es un negocio, hará todo lo que sea posible para economizar dinero. Algunas veces, se arreglan algunas reclamaciones injustificadamente, en mi opinión, antes de terminar el tratamiento adecuado. Además, es increíble que muchos de estos obreros totalmente incapacitados, ayudados por buenas mentes legales y peritos médicos, se convierten en personas capacitadas después que la

cantidad monetaria final ha sido asignada.

Esto no elimina una investigación cuidadosa, tratamiento apropiado, y un estudio científico de signos y síntomas por parte del examinador para que haya un acuerdo justo, a tenor con la ley de compensación de obrero en la comunidad. El examinador no se debe dejar influenciar por los problemas emocionales envueltos y debe solo considerar los hechos ante sus ojos cuando hace el examen final.

Resumen

La evaluación del paciente con incapacidad lumbosacral debe incluir lo siguiente:

- Primero:* El examinador debe tener una historia del accidente, y conocer el historial médico pasado completo del paciente, incluyendo todas las enfermedades y lesiones.
- Segundo:* El debe estar familiarizado con el status social y económico del paciente y su familia.
- Tercero:* El debe conocer el historial pasado de todos los empleos del paciente.
- Cuarto:* El debe estar seguro del diagnóstico y especialmente si hay señales radicales verdaderas presentes. Si hay duda, él debe insistir en que se practique los estudios electromiográficos.
- Quinto:* El debe saber el alcance del tratamiento. ¿Hubo descanso en cama absoluto hasta que desaparecieran los espasmos musculares y las contracturas refleja de los músculos, ejercicios para fortalecer los músculos debilitados y estirar los contraídos, e instrucción adecuada en la postura para prevenir lesiones en la espalda en el futuro?
- Sexto:* En caso de pronóstico dudoso, él debe insistir en una prueba de trabajo, lo mismo en un centro de rehabilitación o en el propio trabajo bajo estricta supervisión.

Luego de haber terminado todos estos estudios estará el médico capacitado para evaluar verdaderamente en término de pérdida de función en el trabajo específico. Finalmente, el hecho de que un obrero está incapacitado para cierto trabajo no quiere decir que él no pueda trabajar. Se le debe dar la oportunidad para entrenamiento vocacional en un ambiente que considere las limitaciones físicas, ambientales, y situacionales en la incapacidad específica antes de cerrar el caso.

Summary

Disability evaluation of the patient with lumbosacral incapacity should include the following facts:

First, the examiner should have a complete history of the present accident, and a full knowledge of the patient's past medical history including past ailments and injuries.

Second, he should be familiar with the social and economic status of the patient and his family.

Third, he should be briefed on the past work history of the patient.

Fourth, he should be certain of the diagnosis, and, especially, if there are true radicular signs. If in any doubt, he should insist on electromyography.

Fifth, he should know the extent of local treatment: complete bed rest until disappearance of muscular

spasm and reflex muscle contractures, exercises to build up weakened muscles and to stretch contracted ones, and proper instruction in posture hints to prevent future low-back injury.

Sixth, in cases of doubtful prognosis, he should insist on a work test, either in a rehabilitation center or on-the-job, under close supervision.

Then, and only then, is the rating physician able to arrive at a true incapacity in terms of the percentage loss of function for that particular job. Finally, the fact that the injured workman is totally incapacitated for one job does not mean he cannot do any work. Provisions for vocational training in an environment which considers the physical, environmental, and situational limitations of the particular disability must be provided before the case is closed.

BOOK REVIEW

Marcial-Rojas:
PATHOLOGY OF PROTOZOAL AND HELMINTHIC
DISEASES

This is the first and only comprehensive book to cover all the major human protozoal and helminthic diseases with the appropriate clinical correlation. Dr. Marcial-Rojas, one of the world's leading authorities on tropical diseases, has utilized his extensive knowledge and experience in writing a good portion of the book himself and has gathered highly qualified specialists to complement his own work. The outcome is a book certainly to be required reading for pathologists and practitioners throughout the world. This first edition is truly a landmark in the recognition of parasitology by the medical profession. It shall go a long way to work making practitioners more conscious and keenly aware of the role parasitic diseases play in the world.

The publishers and authors are to be congratulated for a handsome book and for a very significant achievement.

Ramón H. Bermúdez, MD

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Note: Oral contraceptives are complex medications. As with all medications they should be prescribed with discriminating care, and only after reference to full prescribing information. For brief summary of prescribing information, please see next page.

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Actions—Ovulen and Demulen act to prevent ovulation by inhibiting the output of gonadotropins from the pituitary gland. Ovulen and Demulen depress the output of both the follicle-stimulating hormone (FSH) and the luteinizing hormone (LH).

Special note—Oral contraceptives have been marketed in the United States since 1960. Reported pregnancy rates vary from product to product. The effectiveness of the sequential products appears to be somewhat lower than that of the combination products. Both types provide almost completely effective contraception.

An increased risk of thromboembolic disease associated with the use of hormonal contraceptives has now been shown in studies conducted in both Great Britain and the United States. Other risks, such as those of elevated blood pressure, liver disease and reduced tolerance to carbohydrates, have not been quantitated with precision.

Long-term administration of both natural and synthetic estrogens in subprimate animal species in multiples of the human dose increases the frequency of some animal carcinomas. These data cannot be transposed directly to man. The possible carcinogenicity due to the estrogens can be neither affirmed nor refuted at this time. Close clinical surveillance of all women taking oral contraceptives must be continued.

Indication—Ovulen and Demulen are indicated for oral contraception.

Contraindications—Patients with thrombophlebitis, thromboembolic disorders, cerebral apoplexy or a past history of these conditions, markedly impaired liver function, known or suspected carcinoma of the breast, known or suspected estrogen-dependent neoplasia and undiagnosed abnormal genital bleeding.

Warnings—The physician should be alert to the earliest manifestations of thrombotic disorders (thrombophlebitis, cerebrovascular disorders, pulmonary embolism and retinal thrombosis). Should any of these occur or be suspected the drug should be discontinued immediately.

Retrospective studies of morbidity and mortality conducted in Great Britain and studies of morbidity in the United States have shown a statistically significant association between thrombophlebitis, pulmonary embolism, and cerebral thrombosis and embolism and the use of oral contraceptives. There have been three principal studies in Britain¹⁻³ leading to this conclusion, and one⁴ in the United States. The estimate of the relative risk of thromboembolism in the study by Vessey and Doll³ was about sevenfold, while Sartwell and associates⁴ in the United States found a relative risk of 4.4, meaning that the users are several times as likely to undergo thromboembolic disease without evident cause as non-users. The American study also indicated that the risk did not persist after discontinuation of administration and that it was not enhanced by long-continued administration. The American study was not designed to evaluate a difference between products. However, the study suggested that there might be an increased risk of thromboembolic disease in users of sequential products. This risk cannot be quantitated, and further studies to confirm this finding are desirable.

Discontinue medication pending examination if there is sudden partial or complete loss of vision, or if there is a sudden onset of proptosis, diplopia or migraine. If examination reveals papilledema or retinal vascular lesions medication should be withdrawn.

Since the safety of Ovulen and Demulen in pregnancy has not been demonstrated, it is recommended that for any patient who has missed two consecutive periods pregnancy should be ruled out before continuing the contraceptive regimen. If the patient has not adhered to the prescribed schedule the possibility of pregnancy should be considered at the time of the first missed period.

A small fraction of the hormonal agents in oral contraceptives has been identified in the milk of mothers receiving these drugs. The long-range effect to the nursing infant cannot be determined at this time.

Precautions—The pretreatment and periodic physical examinations should include special reference to the breasts and pelvic organs, including a Papanicolaou smear since estrogens have been known to produce tumors, some of them malignant, in five species of subprimate animals. Endocrine and possibly liver function tests may be affected by treatment with Ovulen or Demulen. Therefore, if such tests are abnormal in a patient taking Ovulen or Demulen, it is recommended that they be repeated after the drug has been withdrawn for two months. Under the influence of progestogen-estrogen preparations preexisting uterine fibromyomas may increase in size. Because these agents may cause some degree of

fluid retention, conditions which might be influenced by this factor, such as epilepsy, migraine, asthma, cardiac or renal dysfunction, require careful observation. In breakthrough bleeding, and in all cases of irregular bleeding per vaginam, nonfunctional causes should be borne in mind. In undiagnosed bleeding per vaginam adequate diagnostic measures are indicated. Patients with a history of psychic depression should be carefully observed and the drug discontinued if the depression recurs to a serious degree. Any possible influence of prolonged Ovulen or Demulen therapy on pituitary, ovarian, adrenal, hepatic or uterine function awaits further study. A decrease in glucose tolerance has been observed in a significant percentage of patients on oral contraceptives. The mechanism of this decrease is obscure. For this reason, diabetic patients should be carefully observed while receiving Ovulen or Demulen therapy. The age of the patient constitutes no absolute limiting factor, although treatment with Ovulen or Demulen may mask the onset of the climacteric. The pathologist should be advised of Ovulen or Demulen therapy when relevant specimens are submitted. Susceptible women may experience an increase in blood pressure following administration of contraceptive steroids.

Adverse reactions observed in patients receiving oral contraceptives—A statistically significant association has been demonstrated between use of oral contraceptives and the following serious adverse reactions: thrombophlebitis, pulmonary embolism and cerebral thrombosis.

Although available evidence is suggestive of an association, such a relationship has been neither confirmed nor refuted for the following serious adverse reactions: neuro-ocular lesions, e.g., retinal thrombosis and optic neuritis.

The following adverse reactions are known to occur in patients receiving oral contraceptives: nausea, vomiting, gastrointestinal symptoms (such as abdominal cramps and bloating), breakthrough bleeding, spotting, change in menstrual flow, amenorrhea during and after treatment, edema, chloasma or melasma, breast changes (tenderness, enlargement and secretion), change in weight (increase or decrease), changes in cervical erosion and cervical secretions, suppression of lactation when given immediately post partum, cholestatic jaundice, migraine, rash (allergic), rise in blood pressure in susceptible individuals and mental depression.

Although the following adverse reactions have been reported in users of oral contraceptives, an association has been neither confirmed nor refuted: anovulation post treatment, premenstrual-like syndrome, changes in libido, changes in appetite, cystitis-like syndrome, headache, nervousness, dizziness, fatigue, backache, hirsutism, loss of scalp hair, erythema multiforme, erythema nodosum, hemorrhagic eruption and itching.

The following laboratory results may be altered by the use of oral contraceptives: hepatic function: increased sulfobromophthalein retention and other tests; coagulation tests: increase in prothrombin, Factors VII, VIII, IX and X; thyroid function: increase in PBI and butanol extractable protein bound iodine, and decrease in T₃ uptake values; metyrapone test and pregnanediol determination.

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The Special Note, Contraindications, Warnings, Precautions and Adverse Reactions listed above for Ovulen and Demulen are applicable to Enovid-E and should be observed when prescribing Enovid-E.

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QUO VADIS

La frase "Quo Vadis" se conoce por una novela, y por una película, que describen cómo San Pedro, al huir de Roma por saberse perseguido por las autoridades, oye la voz del Señor que con un sencillo "¿A Dónde Vas?" lo hace parar, reflexionar y volver a enfrentarse a sus enemigos.

No creo sea el momento de entrar en una explicación teológica de este encuentro, pero sí el de que cada uno nos preguntemos ¿A Dónde Vas?. No podemos cerrar los ojos a las críticas de que estamos siendo objeto y a los cambios que se avecinan.

Se nos acusa, entre otros, de mercaderes de la salud. La frase de que los costos son exagerados y que todos los médicos somos millonarios, se ha repetido tantas veces que casi todo el mundo se lo cree (menos yo).

Los costos de hospitalización sí han aumentado considerablemente, pero éstos dependen de muchos factores no médicos: empleados, suplidos, comida, etc. Los costos al médico no han aumentado ni tan siquiera al ritmo del alza del costo de la vida.

Lo que los economistas nos pueden echar en cara, y esto no es culpa nuestra, es que el producto . . . la salud . . . es un renglón de primera necesidad y siempre existente, pues nuestros clientes no tienen que estar enfermos para venirnos a consultar. Si por esta premisa de economía se nos culpa de mercaderes en salud yo sólo puedo contestar: "La salud no es un producto agrícola ni industrial, ni se anuncia, ni se vende. No se puede tratar dentro de los postulados de la economía".

Por esta y otras muchas acusaciones mal intencionadas se habla de que existe una crisis en salud y para algunos, la única solución consiste en cambiar radicalmente toda la organización médico-hospitalaria y entregarla atada de pies y manos al Estado, para que la dirija y administre. Y a esta situación nos enfrentamos actualmente.

La reacción a un suceso alarmante e inesperado puede ser una de tres: huida en estampida, inmovilidad que puede ser transitoria o permanente, o enfrentamiento y solución al suceso.

A los médicos nos han entrenado para enfrentarnos a todo tipo de emergencia. Muchos al principio hemos tenido nuestros momentos de inmovilidad para luego actuar según lo aprendido. El tiempo hasta nos ha enseñado a huir defensivamente, pero no para rehuir el problema, sino para ganar tiempo para combatir mejor.

El momento es uno de pensamiento introspectivo profundo y de unión profesional. San Pedro volvió y se enfrentó a sus enemigos y fue crucificado . . . pero sus creencias y religión han subsistido a través de los siglos. ¿Estamos nosotros preparados para un sacrificio similar?

¡Que la conciencia de cada cual los guíe y que no tengan que arrepentirse después!

Rosa E. Fiol, MD



DRA. ROSA E. FIOL

Presidenta, Asociación Médica de Puerto Rico

1973

La Dra. Rosa E. Fiol nació en Santurce, Puerto Rico, realizando sus estudios primarios y secundarios en Nueva York, Islas Vírgenes y Puerto Rico. En el 1948 recibió su título de Bachiller en Ciencias de la Universidad de Puerto Rico. En ese mismo año se trasladó a la República Dominicana (1948-52) donde comenzó su carrera de medicina. En el 1952 viaja a España donde termina dichos estudios, recibiendo su título de Doctor en Medicina de la Universidad Central de Madrid en el 1953.

Inmediatamente regresa a Puerto Rico haciendo su año de internado en el Hospital Municipal de Río Piedras, y una residencia en Medicina Interna en el Hospital de Veteranos del Bronx, Nueva York, especializándose en Patología, y del 1957-59 en Neuropatología del Columbia Presbyterian Hospital, Nueva York.

La doctora Fiol es la única Neuropatóloga en Puerto Rico y actualmente se desempeña en la Sección de Neurología y Departamento de Patología de la Escuela de Medicina de la Universidad de Puerto Rico, y como Profesora Asociada en Neuropatología. Es además Jefe del Laboratorio de Patología del Hato Rey Psychiatric Hospital.

La doctora Fiol es miembro de las siguientes Asociaciones Profesionales:

American Association of Neuropathologists

Sociedad de Patólogos de Puerto Rico

Sección de Siquiatría, Neurología y Neurocirugía de la AMPR

Alianza Panamericana de Mujeres Médicos

Asociación Americana de Mujeres Médicos

Asociación de Mujeres Médicos de Puerto Rico

Academia Puertorriqueña de Neurología

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En este año a punto de terminar, la Junta Editora desea expresar su agradecimiento a nuestros patrocinadores del Boletín de la Asociación Médica de Puerto Rico, quienes con su apoyo, permiten nuestra labor y el logro de nuestros objetivos. Son éstos proveer un medio para la publicación de artículos científicos de nuestros médicos, informar a nuestros lectores de problemas médicos de importancia, proporcionar vías de comunicación para expresar puntos de vista; tanto oficiales como de índole personal, estimular liderato médico para la solución de nuestros problemas; en fin, lograr una revista de actualidad que refleje la calidad de la medicina Puertorriqueña.

Agradecemos la ayuda y apoyo de nuestros patrocinadores.

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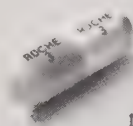
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